8/3,AB/1
DIALOG(R)File 155:MEDLINE(R)


11251480 98129051 PMID: 9467870

Uteroferrin and recombinant bovine GM-CSF modulate the my losuppressive effects of 5-fluorouracil in young female pigs (Sus scrofa).

Laurenz J C; Hadjisavas M; Schuster D; Bazer F W
Department of Animal Science, Texas A&M University, College Station 77843-2471, USA.

Comparative biochemistry and physiology. Part B, Biochemistry & molecular biology (ENGLAND) Nov 1997, 118 (3) p569-77, ISSN 1096-4959
Journal Code: 9516061
Contract/Grant No.: DK 46766; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The present study investigated the ability of uteroferrin and recombinant bovine granulocyte monocyte/macrophage-colony stimulating factor (rbGM-CSF) to modulate the myelosuppressive effects of 5-fluorouracil (5-FU) in young female pigs (Sus scrofa). Pigs (N = 3/treatment) were infused with 5-FU (32.5 mg/kg) on days 0 and 1 of the experimental period. Uteroferrin (100 micrograms/kg in 0.9% NaCl), rbGM-CSF (10 micrograms/kg in 0.9% NaCl), uteroferrin + rbGM-CSF (as above) or control (0.9% NaCl) were administered as intramuscular injections twice daily (0800 and 2000 hr). Peripheral blood cell number, composition, and progenitor cells were determined over 28 days. Treatment of pigs with 5-FU resulted in a rapid leukocytopenia and thrombocytopenia (nadirs on days 5 and 7, respectively) and a modest decrease ($P < 0.05$) in red blood cell (RBC) number (nadir on day 14). Although nor affecting RBC and thrombocytes, treatment of pigs with uteroferrin had an initial protective effect ($P < 0.05$) on the 5-FU-induced leukocytopenia (63 and 64 vs 48 and 39 +/- 6% of baseline on days 3 and 5, respectively). In contrast, rbGM-CSF enhanced ($P < 0.05$) the rate of the leukocytopenia and had only minor ffects on thrombocyte numbers relative to controls. These effects appeared to be additive, as pigs treated with uteroferrin + rbGM-CSF had a reduced rate of leukocytopenia compared to pigs treated with rbGM-CSF alone. Uteroferrin + rbGM-CSF also attenuated ($P < 0.05$) the suppression and enhanced ($P < 0.05$) recovery of RBC and thrombocyte numbers following 5-FU treatment. In control pigs, a modest rebound leukocytosis (122 +/- 6% of baseline) and thrombocytosis (141 +/- 9% of baseline) was evident. Uteroferrin enhanced ($P < 0.05$) the rebound leukocytosis (135 +/- 6% of baseline), but attenuated ($P < 0.05$) the thrombocytosis. In contrast, rbGM-CSF enhanced ($P < 0.05$) the duration of the leukocytosis during the r covery phase, an effect augmented by the combination of uteroferrin + rbGM-CSF. In addition, treatment with uteroferrin + rbGM-CSF resulted in a sustained thrombocytosis (days 12 to 21). As indicated by changes in CFU-GM, BFU-E, and CFU-GEMM progenitor cells in peripheral blood, the effects of uteroferrin and rbGM-CSF appeared to reflect their ability to enhance the proliferation and/or differentiation of both similar and distinct hematopoietic progenitor cells.

11jun03 06:11:44 User217743 Session D608.1
$0.00 0.161 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.00 Estimated cost this search
$0.00 Estimated total session cost 0.161 DialUnits
File 410:Chronolog(R) 1981-2003/Mar
(c) 2003 The Dialog Corporation

Set Items Description
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? b 155
11jun03 06:11:51 User217743 Session D608.2
$0.00 0.071 DialUnits File410
$0.00 Estimated cost File410
$0.03 TELNET
$0.03 Estimated cost this search
$0.03 Estimated total session cost 0.232 DialUnits
File 155:MEDLINE(R) 1966-2003/Jun W1
(c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.

Set Items Description
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? s leukocytosis and thrombocytopenia
6230 LEUKOCYTOSIS
24787 THROMBOCYTOPENIA
S1 355 LEUKOCYTOSIS AND THROMBOCYTOPENIA
? s s1/ti
S2 28 S1/TI
? t s2/3,ab/all

2/3,AB/1
DIALOG(R)File 155:MEDLINE(R)
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13894326 22033950 PMID: 12038519
Co-existence of *thrombocytopenia* and hyperleukocytosis ('critical period') as a risk factor of haemorrhage into the central nervous system in patients with acute leukaemias.
Nowacki Przemyslaw; Zdziarska Barbara; Fryze Cezary; Urasinski Ignacy; et al
Department of Neurology, Pomeranian Medical University, Szczecin, Poland. Haematologia (Netherlands) 2002, 31 (4) p347-55, ISSN 0017-6559 Journal Code: 0130266
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The aim of this work was to examine whether the risk of death i.a. due to haemorrhage into the central nervous system (CNS) is higher during some phases of acute myeloblastic leukaemia (AML), lymphoblastic leukaemia (ALL), and the blastic phase of chronic myelogenous leukaemia (BP) when two important risk factors that worsen the prognosis are simultaneously present: low thrombocytopenia and hyperleukocytosis. Clinical and post-mortem neuropathological examination was performed in 143 patients, aged 17-76 years, who died from AML (80 cases), BP (38), and ALL (25). Periods with co-existence of thrombocytopenia below 25 x 10(9) per l and hyperleukocytosis above 100 x 10(9) per l were identified after plotting the results and were termed the 'critical period' (CP). The study showed that the risk of death was disproportionately high during the CP. This finding was obtained in all patient groups, although it involved mainly patients with AML and BP, i.e. leukaemias with the highest frequency of hyperleukocytosis in peripheral blood. It is suggested that the risk of death during the CP is so high because leukaemic cells are a potent synergistic factor to thrombocytopenia in causing CNS haemorrhage. When a CP is detected, hyperleukocytosis and thrombocytopenia should be controlled and treated aggressively: leukapheresis and platelet concentrates should be administered. Patients with CP should not be given packed red blood cells, in order to avoid a further increase in blood viscosity, which is already high due to hyperleukocytosis. In fact, anaemia during the CP should be regarded as a potentially life-saving factor.

2/3,AB/2
DIALOG(R)File 155:MEDLINE(R)
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11953674 99397932 PMID: 10467277
Carbamazepine-induced *thrombocytopenia* defined by a challenge test. Ishikita T; Ishiguro A; Fujisawa K; Tsukimoto I; Shimbo T Department of Pediatrics, Mizonokuchi Hospital, Teikyo University School of Medicine, Kawasaki, Japan.
American journal of hematology (UNITED STATES) Sep 1999, 62 (1) p52-5, ISSN 0361-8609 Journal Code: 7610369
Document type: Journal Article; Review; Review of Reported Cases Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Carbamazepine (CBZ), a widely used anticonvulsant, occasionally causes serious hematologic disorders. A 12-year-old boy was admitted because of a diffuse petechial rash and profound thrombocytopenia (10 x 10(9) platelets/l), after having been treated for epilepsy with CBZ for 12 days. Seven days following withdrawal of CBZ and initiation of prednisolone therapy, the

platelet count recovered. In a subsequent challenge test with CBZ, platelet counts again decreased, and the levels of platelet-associated IgG and serum interleukin-6 increased. No antibodies against platelet glycoprotein IIb/IIIa or Ib were detected in plasma. We believe that this is the first reported occasion when CBZ-induced thrombocytopenia has been defined by a rechallenge test. 

2/3,AB/3
DIALOG(R)File 155:MEDLINE(R)


10670594 97019669 PMID: 8866143
Retinal findings in adult leukaemia: correlation with *leukocytosis*.
Jackson N; Reddy S C; Hishamuddin M; Low H C
Department of Medicine, Universiti Sains Malaysia, Kelantan, Malaysia. Clinical and laboratory haematology (ENGLAND) Jun 1996, 18 (2) p105-9, ISSN 0141-9854 Journal Code: 7907061
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The associations between retinal findings and haematological parameters in acute leukaemia are controversial. Sixty-three newly-diagnosed acute leukaemia patients, aged 12-77 years, were studied prospectively for the presence of intra-retinal haemorrhages (IRH), white-centred haemorrhages (WCH), cotton wool spots (CWS) and macular haemorrhages (MH), Thirty-three patients (52.4%) showed at least one retinal abnormality. The prevalence of individual findings was: IRH (30 cases), WCH (20 cases), CWS (5 cases), MH (11 cases). In contrast to previous studies, there was no association between any of these retinal findings and the haemoglobin level or the platelet count. There was a higher median WBC in patients with IRH (68 x 10(9)/l) than in those without IRH (15.4 x 10(9)/l), P = 0.037. When the acute myeloblastic leukaemia cases were considered separately, an association was also found between higher WBC and the presence of WCH and CWS. There was no association between retinal findings and FAB type in the AML cases. We conclude that a high WBC may be at least as important as anaemia and thrombocytopenia in the pathogenesis of the retinopathy of acute leukaemia.

2/3,AB/4
DIALOG(R)File 155:MEDLINE(R)


10591346 96406415 PMID: 8810548
An autopsy case of systemic lupus erythematosus complicating *leukocytosis*, amegakaryocytic *thrombocytopenia* , interstitial pneumonitis, and pleulitis]
Kawamoto A; Shiiki H; Hanatani M; Hashimoto T; Dohi K
First department of internal medicine, Nara medical university. Nihon Rinsho Men'eki Gakkai kaishi = Japanese journal of clinical immunology (JAPAN) Jun 1996, 19 (3) p223-31, ISSN 0911-4300 Journal Code: 9505992
Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
A 52-year-old female was admitted to our hospital in August 1988, for evaluation of purpura and gingival bleeding. Hematologic examination showed mild leukocytosis (12,400/microliter) and severe thrombocytopenia (1,000/microliter). On bone marrow examination, megakaryocyte count was normal and the number of myeloblasts was increased (7.2%). Serological examination was positive for anti-nuclear antibody and anti-DNA antibody. She was diagnosed as having idiopathic or autoimmune thrombocytopenia, and received thrombocyte transfusion and gamma-globulin administration. Hematologic values improved temporarily, but leukocytosis and thrombocytopenia recurred. On the 22nd hospital day, leukocytes increased to 49,300/microliter and thrombocytes decreased to 10,000/microliter. Bone marrow myeloblasts were also increased to 18.8%, and she was suspected of having myelodysplastic syndrome. Then, hematologic values improved simultaneously, and she was discharged in November 1988. After the discharge, leukocyte count ranged from 6,000 to 16,500/microliter, but the number of bone marrow myeloblasts was normal. However, transient thrombocytopenia appeared in association with decrease or absence of bone marrow megakaryocytes and rise of platelet associated-IgG, (PA-IgG) to 99.6 ng/10(7) cells. From September to December 1989, she complained of fever, morning stiffness, multiple arthralgia, and oral ulcer. On serological findings, she was positive for LE cell. Therefore, she was diagnosed as having systemic lupus erythematosus (SLE). In January 1990, she had a high grade fever and dyspnea. Bilateral pleuritis and interstitial pneumonitis were shown on the chest roentgenogram. She received gamma-globulin administration, methylprednisolone pulse therapy, and mechanical ventilation. However, hypoxia developed rapidly, and she died of respiratory failure. Autopsy revealed severe interstitial pneumonitis, fibrinous pleuritis, fibrinous pericarditis, and vasculitis in the arcuate artery of the kidney. This is the first report of SLE complicating thrombocytopenia associated with decrease of megakaryocytes and rise of the PA-IgG, and severe leukocytosis associated with increased

bone marrow myeloblasts.

2/3,AB/5
DIALOG(R)File 155:MEDLINE(R)
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09170420 20475199 PMID: 11020995
Progression of refractory *thrombocytopenia* to chronic myelomonocytic leukemia accompanied by various inflammatory reactions] Gomyo H; Murayama T; Kohfuku J; Mizuno I; Kajimoto K; Koizumi T; Imoto S Department of Medicine, Hyogo Medical Center for Adults. Rinsho ketsueki The Japanese journal of clinical hematology (JAPAN) Aug 2000, 41 (8) p664-70, ISSN 0485-1439 Journal Code: 2984782R Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
A 51-year-old man was admitted for treatment of severe thrombocytopenia in May 1997. A diagnosis of MDS RA (refractory thrombocytopenia; RTC) was made by bone marrow examination, which revealed mild marrow hypoplasia and a reduced number of megakaryocytes accompanied by micromegakaryocytes and hypolobular megakaryocytes. Chromosome analysis demonstrated 46, XY, t(5;7) (q31;q22) in all 20 cells examined. The patient received only supportive therapy including platelet transfusion, until leukocytosis and monocytosis gradually developed in November 1998. In view of a marked increase in the number of monocytes (more than 3,000/microliter), a diagnosis of CMML was made in December 1998. As the leukocytosis progressed, various inflammatory symptoms such as facial erythema and endophthalmitis developed. Administration of interferon alpha (IFN alpha) unexpectedly worsened the leukocytosis and monocytosis, suggesting abnormal responses of these cells to IFN alpha. Detailed molecular analysis of these cells might reveal a novel mechanism of leukemogenesis associated with 5q31.

2/3,AB/6
DIALOG(R)File 155:MEDLINE(R)
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09157390 20459918 PMID: 11005136
Atypical process of acute disturbance of liver function with severe *thrombocytopenia* in the third trimester]
Atypischer Verlauf einer akuten Leberfunktionsstorung mit schwerer Thrombozytopenie im dritten Trimester.
Rigo J; Tanyi J; Varga I; Gorbe E
Klinik fur Geburtshilfe und Frauenheilkunde, Semmelweis Medizinische Universitat, Budapest Ungarn.
Zentralblatt fur Gynakologie (GERMANY) 2000, 122 (8) p436-8, ISSN 0044-4197 Journal Code: 21820100R
Document type: Journal Article ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed
The authors diagnosed disturbance of liver-function associated with severe thrombopenia in a pregnant woman in the third trimester. Principally, acute fatty liver of pregnancy can be characterized by existing symptoms, e.g. nausea, vomiting, epigastric pain, jaundice, hyperbilirubinemia, moderately elevated SGOT and SGPT levels, thrombopenia, leukocytosis, low fibrinogen level and disseminated intravascular coagulopathy, but hepatomegaly, purpura and petechia on lower and upper extremities, and high ALP and GGT levels during postpartum period do not confirm suspicion of this diagnosis. The present report draws attention to the difficulties of differential diagnosis of pregnancy-induced elevated liver enzymes diseases associated with low platelets, as there are several identical pathophysiological processes. Although causes and exact pathophysiology of disorders are unknown, similar symptoms during the process of diseases leave the question open whether they are different diseases or whether they are different manifestations of the same disease, and what kind of relationship exists between these diseases and preeclampsia. This case suggests careful evaluation of the whole clinical picture, moreover it is emphasized that prompt, aggressive treatment of hemostatic disturbance and the expeditious delivery can save maternal life.

2/3,AB/7
DIALOG(R)File 155:MEDLINE(R)
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09118654 20417496 PMID: 10963506
*Leukocytosis* is proportional to HELLP syndrome severity: evidence for an inflammatory form of preeclampsia.
Terrone D A; Rinehart B K; May W L; Moore A; Magann E F; Martin J N Department of Obstetrics and Gynecology, University of Mississippi Medical Center, Jackson 39216-4505, USA.
Southern medical journal (UNITED STATES) Aug 2000, 93 (8) p768-71, ISSN 0038-4348 Journal Code: 0404522
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BACKGROUND: We investigated the possibility that HELLP syndrome is in part a systemic inflammatory

response. METHODS: We evaluated total white blood cell (WBC) counts of all patients with severe preeclampsia with and without HELLP syndrome admitted to our hospital between 1995 and 1997. Patients were grouped by diagnosis and timing of platelet nadir. Analysis of variance and regression analysis were used for data analysis. RESULTS: Of 177 patients, 91 had HELLP syndrome, and 86 had severe preeclampsia alone. The WBC counts were significantly higher in patients with HELLP syndrome (12.5 +/- .442 x 10(9)/L) than in patients with severe preeclampsia (10.3 +/- .288 x 10(9)/L). Regression analysis showed that platelet counts varied inversely with WBC counts. Also, patients with class I HELLP syndrome had significantly higher WBC counts than patients with other classes of HELLP syndrome. CONCLUSION: The finding of an association between increasing leukocytosis and worsening thrombocytopenia early in the course of HELLP syndrome supports the hypothesis that it may represent an inflammatory process.

2/3,AB/8
DIALOG(R)File 155:MEDLINE(R)


08619850 95308377 PMID: 7540500
Horse gammaglobulin-induced *thrombocytopenia* in anaphylaxis involving sequestration and activation of platelets.
Leir S H; Chen S H; Lei H Y
Department of Microbiology, College of Medicine, National Cheng Kung University, Tainan, Taiwan, Republic of China.
Clinical and experimental allergy - journal of the British Society for Allergy and Clinical Immunology (ENGLAND) Mar 1995, 25 (3) p273-80, ISSN 0954-7894 Journal Code: 8906443
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Thrombocytopenia as well as hemoconcentration and leukopenia followed by leukocytosis were induced after HoGG challenge on HoGG-sensitized mice. Thrombocytopenia was induced within 2 min and sustained for 1 day. HoGG-induced thrombocytopenia was not observed until day 10 after sensitization; mice challenged with HoGG dose > or = 10 micrograms developed thrombocytopenia. Two types of thrombocytopenia were observed in appropriately sensitized mice. HoGG induced thrombocytopenia at 2 min and 60 min, whereas, alpha-macroglobulin induced thrombocytopenia at 2 min, the platelet count of which returned to normal within 60 min. Poly (Glu60Ala30Tyr10) did not induce thrombocytopenia at 2 min or 60 min. The tracing study by 3H-serotonin labelled platelets demonstrated the 2 min-sequestration of platelets in lungs or livers. The HoGG-induced sequestration of platelets at 2 min was blocked by high dose heparin or Cobra Venom factor. Platelet activation at 60 min was partially inhibited by dexamethasone, rhodostomin synthetic peptide 45-59, or platelet activation factor antagonist (WEB 2086). Furthermore, the thrombocytopenia could be transferred by heat (56 degrees C, 4h) treated immune sera. This suggests that HoGG-induced, non-IgE-mediated thrombocytopenia in anaphylaxis involves sequestration and activation of platelets. The sequestion in lungs occurs within 2 min and can be inhibited by high dose heparin or Cobra Venom factor. The activation of platelets involves platelet activation factor, and fibrinogen receptor.

2/3,AB/9
DIALOG(R)File 155:MEDLINE(R)


08300154 94366428 PMID: 7521936
Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. A newborn boy with petechiae, hepatosplenomegaly, *leukocytosis*, and *thrombocytopenia*. New England journal of medicine (UNITED STATES) Oct 13 1994, 331 (15) p1005-12, ISSN 0028-4793 Journal Code: 0255562
Comment in N Engl J Med. 1995 Feb 23;332(8) 540-1; Comment in PMID 7830747; Erratum in N Engl J Med 1994 Dec 8;331(23):1599
Document type: Clinical Conference; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

2/3,AB/10
DIALOG(R)File 155:MEDLINE(R)


08181541 94247462 PMID: 8190136
Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 24-1994. A two-year-old boy with *thrombocytopenia*, *leukocytosis*, and hepatosplenomegaly. New England journal of medicine (UNITED STATES) Jun 16 1994, 330 (24) p1739-46, ISSN 0028-4793 Journal Code: 0255562
Document type: Clinical Conference; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

2/3,AB/11
DIALOG(R)File 155:MEDLINE(R)
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08135917 94201786 PMID: 8151314
Effects of interleukin-1 alpha on carboplatin-induced *thrombocytopenia* in patients with recurrent ovarian cancer. Vadhan-Raj S; Kudelka A P; Garrison L; Gano J; Edwards C L; Freedman R S; Kavanagh J J
Department of Clinical Immunology and Biological Therapy, University of Texas M.D. Anderson Cancer Center, Houston 77030.
Journal of clinical oncology - official journal of the American Society of Clinical Oncology (UNITED STATES) Apr 1994, 12 (4) p707-14, ISSN 0732-183X Journal Code: 8309333
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
PURPOSE: The purpose of this study was to evaluate the clinical safety and ability of interleukin-1 alpha (IL-1 alpha) to ameliorate carboplatin-induced thrombocytopenia and thus allow patients with ovarian cancer to receive multiple cycles of chemotherapy at full doses. PATIENTS AND METHODS: IL-1 alpha was administered by continuous intravenous infusion daily at doses of 0.1 to 10 micrograms/m2/24 hours over 4 days (96 hours) before the first cycle and/or following the second cycle of carboplatin in 21 patients with recurrent ovarian cancer who had platinum-responsive disease. In cycle no. 1, patients received carboplatin (400 mg/m2) alone, while in cycle no. 2 carboplatin was followed by IL-1 alpha. RESULTS: Treatment with IL-1 alpha before carboplatin was associated with moderate leukocytosis (baseline mean, 6.15 x 10(3)/microL; maximum mean, 17.9 x 10(3)/microL; P < .001) and significant increases in platelet counts (baseline mean, 241 x 10(3)/microL; maximal mean, 392 x 10(3)/microL; P < .001). IL-1 alpha following carboplatin significantly reduced the duration of thrombocytopenia (days platelet count < 50,000, 5.1 to 2.9 days; P = .003) and increased the area under the curve (AUC) of platelets as a function of time (P < .001). The mean nadir platelet counts were 54,000/microL and 67,000/microL (P = .08) in cycles no. 1 and 2, respectively. In fact, seven of 12 patients given 3 micrograms/m2/d of IL-1 alpha had less thrombocytopenia in cycle no. 2 than in cycle no. 1. Treatment with IL-1 alpha was associated with the tolerance of multiple cycles of carboplatin at the same dose in several patients. The maximum-tolerated dose (MTD) was 3 micrograms/m2/d; fever, chills, hypotension, and fluid retention were dose-limiting toxic effects. CONCLUSION: These findings demonstrate that IL-1 alpha can enhance recovery of platelets following carboplatin therapy and suggest a potential therapeutic role for IL-1 alpha in attenuating thrombocytopenia associated with chemotherapy.

2/3,AB/12
DIALOG(R)File 155:MEDLINE(R)
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07921641 93382473 PMID: 8257528
Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 40-1993. A 61-year-old woman with jaundice, anemia, *thrombocytopenia*, and *leukocytosis*. New England journal of medicine (UNITED STATES) Oct 7 1993, 329 (15) p1108-15, ISSN 0028-4793 Journal Code: 0255562
Erratum in N Engl J Med 1993 Dec 16;329(25) 1904
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

2/3,AB/13
DIALOG(R)File 155:MEDLINE(R)
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07669453 93124698 PMID: 1479703
Eosinophilic leukemia with cyclic eosinophilic *leukocytosis*] Sada E; Yanagisawa K; Hasegawa H; Fujita S; Kobayashi Y; Kono H; Kondo T First Department of Internal Medicine, Faculty of Medicine, Ehime University.
Rinsho ketsueki The Japanese journal of clinical hematology (JAPAN) Dec 1992, 33 (12) p1884-9, ISSN 0485-1439 Journal Code: 2984782R Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
A 36-year-old male was admitted to the Ehime University Hospital with anemia, eosinophilia and hepatosplenomegaly. Peripheral blood examination demonstrated severe anemia (Hb 7.1g/dl), thrombocytopenia (Plt 6.8 x 10(4)/microliters) and increase of peripheral leukocyte counts (53,000/microliters) with 32.0% of eosinophils which had lobulated nuclei, abnormal distribution of eosinophilic granules and a few vacuoles. The level of serum IgE was low (< 5IU/ml), while that of serum vitamin B12 was elevated. A diagnosis of eosinophilic leukemia was made. He was noted to have spontaneous fluctuations in his eosinophil and total leukocyte counts. To analyze the

mechanism of cyclic eosinophilic leukocytosis, we examined eosinophil colony stimulating activity of the serum and plasma of the patient. These examination showed that eosinophil colony-stimulating activity was not found in his serum and plasma, and cyclic eosinophilic leukocytosis was due to the hemopoietic stem cell disorder.

2/3,AB/14
DIALOG(R)File 155:MEDLINE(R)
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07608574 93063646 PMID: 1436342
Hypocomplementemia and *leukocytosis* in diarrhea-associated hemolytic uremic syndrome.
Robson W L; Leung A K; Fick G H; McKenna A I
Department of Pediatrics, University of Calgary, Alta., Canada. Nephron (SWITZERLAND) 1992, 62 (3) p296-9, ISSN 0028-2766 Journal Code: 0331777
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Sixty-eight children with diarrhea-associated hemolytic uremic syndrome (D+HUS) were retrospectively examined to assess clinical variables associated with the combination of leukocytosis and hypocomplementemia. There was a statistically significant association between the white blood cell count (WBC) and the level of the third component of the complement system (C3). Children with both a low C3 and a high WBC were significantly younger and required hospitalization for a significantly longer period of time. Although there were also trends to increases in the presence of anuria and central nervous system complications and in the duration of anuria, elevated WBC, thrombocytopenia, dialysis, and hemorrhagic colitis in children with both an elevated WBC and a low C3, these changes did not achieve statistical significance. The presence of a low C3 and an elevated WBC may indicate a subset of children with D+HUS with a more severe episode.

2/3,AB/15
DIALOG(R)File 155:MEDLINE(R)
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07510110 92373815 PMID: 1507272
*Thrombocytopenia* and *leukocytosis* induced by single intravenous injections of cadmium-saturated metallothioneins-I and -II in rats.
Hayashi T; Sudo J
Department of Toxicology and Clinical Pharmacology, Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen University, Hokkaido, Japan. Journal of toxicological sciences (JAPAN) May 1992, 17 (2) p31-9, ISSN 0388-1350 Journal Code: 7805798
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To comparably investigate hemotoxic potentials of CdCl2, cadmium-saturated metallothioneins-I (Cd-MT-I) and -II (Cd-MT-II), rats received single intravenous injections of one of those dissolved in saline with equivalent concentrations of Cd (0, 0.1, 0.3 and 1.0 mg Cd/kg body weight), and blood for hematological examinations was sampled at 1 and 5 days (Days 1 and 5) after the administrations. The counts of white blood cells showed dose-dependent increments in the 0.3 and 1.0 mg Cd/kg groups in Cd-MT-I and Cd-MT-II at Day 1, and returned to the normal levels at Day 5. The counts of platelets showed dose-dependent decrements in the three-doses groups of Cd-MT-I and Cd-MT-II at Day 1, and did a returning- and further increasing tendency at Day 5. The counts of red blood cells, values of hematocrit, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration, showed only slight and sporadic changes at Days 1 and 5. As to that thrombocytopenia and leukocytosis were dose-dependently brought by Cd-MTs and not by CdCl2, and as to that CdCl2 and Cd-MTs hardly affected erythrocytes regarding their counts, sizes, hemoglobin contents etc., etiological mechanism (s) remains to be explored. However, our findings should be clinically emphasized in relation to Itai-Itai disease and Cd-intoxication.

2/3,AB/16
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07470226 92333772 PMID: 1630025
CML with autoimmune *thrombocytopenia* observed in the course of IgG (kappa) type monoclonal gammopathy]
Nakase T; Matsuoka N; Iwasaki E; Ukyo S; Shirakawa S
Department of Internal Medicine, Kyoto Yawata Hospital.
Rinsho ketsueki The Japanese journal of clinical hematology (JAPAN) May 1992, 33 (5) p706-8, ISSN 0485-1439 Journal Code: 2984782R Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
An 80-year-old male with IgG (kappa) type benign monoclonal gammopathy was admitted to our hospital because of marked leukocytosis. At the time of admission, thrombocytopenia was also noted. A bone marrow aspirate showed marked granulocytosis with a normal

megakaryocyte count. PAIgG was elevated and the NAP score was low. Ph1 chromosome and rearrangement of the breakpoint cluster region were detected. On the basis of these findings, he was diagnosed as having CML with autoimmune thrombocytopenia. This case was of interest with respect to blood cell differentiation and immunological findings.

2/3,AB/17
DIALOG(R)File 155:MEDLINE(R)


06704457 90330425 PMID: 2376485
Patient with anemia, thrombopenia and slight *leukocytosis*] Patientin mit Anamie, Thrombopenie und geringer Leukozytose. Clemm C; Wick M; Bartl R; Goebel M; Kolb H J
Medizinische Klinik III, Ludwig-Maximilians-Universitat Munchen. Der Internist (GERMANY, WEST) Jun 1990, 31 (6) p423-6, ISSN 0020-9554 Journal Code: 0264620
Document type: Journal Article
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed

2/3,AB/18
DIALOG(R)File 155:MEDLINE(R)


06023622 89038411 PMID: 3141709
A patient with mevalonic aciduria presenting with hepatosplenomegaly, congenital anaemia, *thrombocytopenia* and *leukocytosis*. de Klerk J B; Duran M; Dorland L; Brouwers H A; Bruinvis L; Ketting D
University Children's Hospital Het Wilhelmina Kinderziekenhuis, Utrecht, The Netherlands.
Journal of inherited metabolic disease (ENGLAND) 1988, 11 Suppl 2 p233-6, ISSN 0141-8955 Journal Code: 7910918
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

2/3,AB/19
DIALOG(R)File 155:MEDLINE(R)


05353206 87031416 PMID: 3464525 Record Identifier: 043406; 00185266 *Thrombocytopenia* following intracervical prostaglandin priming] Thrombozytopenie nach intrazervikalem Prostaglandin-Priming. Seufert R; Bartzke G; Casper F; Bauer H
Geburtshilfe und Frauenheilkunde (GERMANY, WEST) Sep 1986, 46 (9) p656-7, ISSN 0016-5751 Journal Code: 0370732
TJ: GEBURTSHILFE UND FRAUENHEILKUNDE.
Document type: Journal Article ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Other Citation Owner: PIP; POP
Abstract Source: PIP
Record type: Completed
Thrombocyte aggregation with normochromic anaemia occurred in a gravida III of 27 years of age with sonographically confirmed foetal hydrocephalus, after prostaglandin E2 cervical priming. The authors discuss the differential diagnostic possibilities, but the actual genesis of the changes remains unclear. Hence, it is recommended to check with particular care especially in induction of abortion, the coagulation system with the thrombocytes, over and above the well-known prostaglandin side effects. Special attention must be paid to the occurrence of allergic reactions, and it must always be borne in mind that induction of abortion after the 14th week of gestation is a risky matter (1).
Because of a hydrocephalic fetus, the 27 year old mother opted for abortion. This was done in the 21st week of pregnancy by ordinary intracervical application of 0.25 mg prostaglandin e2 gel. 30 minutes later the patient began to complain of nausea and dyspnea. Laboratory analysis revealed leukocytosis of 20800/ml and thrombocytopenia of 22000/ml, down from 150,000 ml before the procedure. There were no clinical indications of bleeding. The leukocytosis lasted 2 days and thrombocytopenia roughly 6 days. Treatment included administration of acetylsalicylic acid 3 x 0.5 g and dipyrimadol tablets 3 x 25 mg/day. After thrombocyte count was normalized, abortion was induced by means of spasmolysis and oxytocin i.v. In this case partial resorption of the prostaglandin indicates a systemic effect. Since the half life of E and F group prostaglandins is usually 1-3 minutes, and it is almost completely eliminated after passing through the liver and lungs, a direct prostaglandin effect leading to thrombocyte aggregation lasting several days is unlikely. Absence of thrombocyte antibodies point to a drug induced immune process in which the prostaglandin molecule could appear as a hapten. Ultimately the thrombocyte aggregation described here and normochromic anemia are of unclear origin. Changes in the patients' coagulation system are probably of no functional relevance. The initial leukocytosis must be considered a nonspecific immediate reaction.

2/3,AB/20

DIALOG(R)File 155:MEDLINE(R)
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04789187 85095352 PMID: 3966754
Leukemia of large granular lymphocytes: association with clonal chromosomal abnormalities and autoimmune neutropenia, *thrombocytopenia*%% *%, and hemolytic anemia.*
* Loughran T P; Kadin M E; Starkebaum G; Abkowitz J L; Clark E A; Disteche* *C; Lum L G; Slichter S J*
* Annals of internal medicine (UNITED STATES) Feb 1985, 102 (2)* * p169-75, ISSN 0003-4819 Journal Code: 0372351*
* Contract/Grant No.: CA 31615; CA; NCI; CA 34199; CA; NCI; HL 31641; HL;* *NHLBI; +*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Three patients had leukocytosis of large granular lymphocytes and chronic* *neutropenia. Clonal chromosomal abnormalities (trisomy 8 and trisomy 14)* *and lymphocytic infiltration of splenic red pulp, hepatic sinusoids, and* *bone marrow indicated the neoplastic nature of the large granular* *lymphocytes. Demonstration of a T3+, T8+, HNK-1 + phenotype and low natural* *killer cell activity that was augmented by interferon treatment showed the* *leukemic cells to be immature natural killer cells. Multiple autoantibodies* *were present and included rheumatoid factor and antinuclear,* *antineutrophil, antiplatelet, and antierythrocyte antibodies, suggesting a* *defect of B-cell immunoregulation. In addition, in-vitro studies showed* *impaired suppression of immunoglobulin biosynthesis by abnormal cells from* *one patient. Antineutrophil antibodies and absence of direct cell-mediated* *inhibition of granulocyte-macrophage colony formation supported a humoral* *immune mechanism for the neutropenia. In these patients the syndrome of* *splenomegaly, multiple autoantibodies with neutropenia, and lymphocytosis* *of large granular lymphocytes is due to a neoplastic proliferation of* *immature natural killer cells.*
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* 2/3,AB/21*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04724165 85030088 PMID: 6541641*
* Canine idiopathic *thrombocytopenia* : clinical observations and* *long-term follow-up in 54 cases.*
* Williams D A; Maggio-Price L*
* Journal of the American Veterinary Medical Association (UNITED STATES)* *Sep 15 1984, 185 (6) p660-3, ISSN 0003-1488 Journal Code: 7503067* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Idiopathic thrombocytopenia purpura (ITP) was diagnosed in 54 dogs.* *Bleeding was associated with platelet counts less than or equal to* *30,000/mm3, and occurred most frequently at mucosal surfaces and in the* *skin. Other hematologic changes were variable, the most common being* *regenerative anemia with leukocytosis. Bone marrow examination revealed* *variable megakaryocyte numbers, but hyperplasia was most commonly observed.* *Results of the platelet factor 3 test were positive in only 7 of 25 dogs so* *tested. Treatment included various combinations of corticosteroid,* *vincristine, cyclophosphamide, and splenectomy. The dogs could be* *classified into 4 groups on the basis of the course of disease: (1) 14 dogs* *that died or were euthanized during the first episode of* *thrombocytopenia, (2) 17 dogs that recovered after a single episode of* *thrombocytopenia (acute ITP), (3) 8 dogs in which thrombocytopenia recurred* *over a period of up to 8 months before recovering (acute, recurrent ITP),* *and (4) 15 dogs that experienced repeated episodes of ITP for periods of up* *to 8 years (chronic ITP).*
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* 2/3,AB/22*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04394713 84036527 PMID: 6632146*
* Spurious *leukocytosis* and *thrombocytopenia*. A dual phenomenon* *caused by clumping of platelets in vitro.*
* Solanki D L; Blackburn B C*
* JAMA - the journal of the American Medical Association (UNITED STATES)* *Nov 11 1983, 250 (18) p2514-5, ISSN 0098-7484 Journal Code: 7501160* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Three patients with spurious thrombocytopenia caused by in vitro clumping* *of platelets also had leukocytosis that was inappropriate for their* *clinical state and could not be verified on examination of a blood smear.* *Serial blood counts and analysis of the platelet and WBC histograms proved* *the "leukocytosis" to be spurious and caused by platelet clumps erroneously* *"recognized" by the counter as white blood cells. In three additional* *patients, the WBC counts increased concomitantly with a decrease in their* *platelet counts but remained within the normal range. Abnormal platelet and* *WBC counts generated by automated cell counters must be verified by* *examination of a blood smear before patients are subjected to unwarranted*

*investigations and therapy.*
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* 2/3,AB/23*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*03576151 81268565 PMID: 7265789*
* Initial treatment of acute childhood leukemia with extreme* **leukocytosis* by blood exchange transfusion -- rheological aspects* *(author's transl)]*
* Initialtherapie extremer Leukozytose bei akuter kindlicher Leukamie durch*
*Blutaustauschtransfusion--Rheologische Aspekte.*
* Klose H J; Kelson S; Schwarzbach K; Janka G; Netzel B; Haas R; Betke K* * Klinische Padiatrie (GERMANY, WEST) May 1981, 193 (3) p172-6, ISSN* *0300-8630 Journal Code: 0326144*
* Document type: Journal Article ; English Abstract*
* Languages: GERMAN*
* Main Citation Owner: NLM*
* Record type: Completed*
* In leukemia patients with extremely high leukocytosis the great number of* *poorly deformable lymphoblasts compared to normally deformable red cells* *greatly influences the flow properties of leukemic blood. The increased* *blood viscosity implies a great risk of disturbance of the microcirculation* *by leukostasis and bleeding. Removal of large amounts of leukemic cells by* *exchange transfusion with fresh blood diminished leukemic cell burden and* *reduced the initial elevated leukocyte counts by more than 50% in 3* *patients. In addition, anemia and thrombocytopenia improved and the* *disturbed plasma coagulation returned to normal. One of the patients with* *additional risk factors treated by exchange transfusion died 8 months after* *diagnosis in hematologic release. The two other patients perform well* *without relapse six and nine months after diagnosis, respectively. Exchange* *transfusion with 150 ml/kg of fresh blood is considered to be of value to* *avoid severe early complications as e.g. massive intracerebral hemorrhage* *observed in 3 other patients and to correct hematological and rheological* *abnormalities in childhood leukemia with extreme leukocytosis. Possible* *favourable effects as to long term prognosis have to be awaited.* **
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* 2/3,AB/24*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*03284410 80239550 PMID: 7395922*
* The IVIC syndrome: a new autosomal dominant complex pleiotropic syndrome* *with radial ray hypoplasia, hearing impairment, external ophthalmoplegia,* *and *thrombocytopenia*.*
* Arias S; Penchaszadeh V B; Pinto-Cisternas J; Larrauri S* * American journal of medical genetics (UNITED STATES) 1980, 6 (1)* * p25-59, ISSN 0148-7299 Journal Code: 7708900*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The IVIC syndrome is an autosomal dominant condition affecting mainly the* *upper limbs. It is described from 19 living members of one family of mostly* *Caucasoid descent; it came to Venezuela from the Canary Islands 140 years* *ago. The new mutation appeared six generations ago. It has complete* *penetrance and wide expressivity for a radial ray defect which may vary* *from an almost normal thumb to a severely malformed upper limb. When* *present, the thumb has a long/slender metacarpal and a short distal* *phalanx, reflected in a typical metacarpophalangeal (MP) pattern profile.* *Anthropometry reveals delayed growth in the forearms, clavicles, and* *cranium during adolescence, and permanently in the spine; the maturation of* *the face, tibiae, and feet is normal. The radial carpal bones are always* *affected, some being still hypoplastic at advanced ages. Constant palmar* *dermatoglyphic anomalies are a high a-b ridge count, a distally placed or* *absent t triradius, and an increased frequency of patterns in the second* *interdigital area. Extraocular muscles are involved almost always,* *producing strabismus. Hearing is bilaterally impaired due to a mixed* *congenital loss, either total or partial. Mild thrombocytopenia and* *leukocytosis are present before the age of 50 years. There is neither* *associated ectodermal dysplasia nor heart involvement [except for* *occasional mild, incomplete right bundle branch block (IRBBB)]; imperforate* *anus occurs in about 10% of affected persons. The possible pathogenetic* *relationship to the thalidomide embryopathy and to the Holt-Oram syndrome,* *among others, is discussed.*
**
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* 2/3,AB/25*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*02706079 78134259 PMID: 273132*
* Extreme leukemic *leukocytosis* (blast crisis) in childhood.* * Dearth J C; Fountain K S; Smithson W A; Burgert E O; Gilchrist G S* * Mayo Clinic proceedings (UNITED STATES) Apr 1978, 53 (4) p207-11,* *ISSN 0025-6196 Journal Code: 0405543*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Children with leukemia who have extremely high leukocyte counts (more* *than 100,000/mm3) when seen initially are at high risk of early sudden* *death,

usually from massive intracerebral hemorrhage. Nine such patients* *were seen during a 39-month period. Eight had pronounced adenopathy and* *hepatosplenomegaly without severe anemia or thrombocytopenia. The first six* *patients died suddenly. Cerebral perivascular infiltration and increased* *blood viscosity are the probable pathophysiologic mechanisms. A treatment* *program was developed, the goal being the early elimination of blast cells.* *Three consecutive patients patients presenting with leukocyte counts* *greater than 100,000/mm3 were treated with emergency cranial irradiation,* *and all three survived to receive systemic chemotherapy.* **
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* 2/3,AB/26*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*01941684 75117284 PMID: 1090770*
* Shiga bacillus dysentery associated with marked *leukocytosis* and* *erythrocyte fragmentation.*
* Rahaman M M; JamiulAlam A K; Islam M R; Greenough W B** * Johns Hopkins medical journal (UNITED STATES) Feb 1975, 136 (2)* * p65-70, ISSN 0021-7263 Journal Code: 0072456*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Granulocytic leukemoid reactions (white blood cell counts greater than* *50,000 with myelocytes and promyelocytes in the peripheral blood) were* *documented in 15 per cent of 273 patients with dysentery due to Shigella* *dysenteriae, type 1 (Shiga bacillus) in Bangladesh. Peak granulocytosis* *occurred during the second week of illness, when the children were commonly* *afebrile and diarrhea had ceased or was subsiding. More than half of the* *patients with leukemoid reactions subsequently developed a fall in* *hematocrit associated with striking erythrocyte fragmentation on blood* *smears. Thrombocytopenia occurred during the period of hemolysis in most.* *Transient oliguric renal failure developed in several patients. Most made a* *complete recovery. The pathogenesis of the syndrome and the reason for its* *high incidence were not determined.*
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* 2/3,AB/27*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*01350447 72228881 PMID: 5151281*
* Congenital hypoplastic *thrombocytopenia* with radial aplasia.* *Description of a case]*
* La thrombocytopenie hypoplastique congenitale avec aplasie radiale.* *Description d'un cas.*
* Masson A; Cronmuller G; Rousselot P; Lutz D; Berger J; Schneegans E** * Annales de pediatrie (FRANCE) Dec 14 1971, 18 (12) p777-88, ISSN* *0066-2097 Journal Code: 2984696R*
* Document type: Journal Article*
* Languages: FRENCH*
* Main Citation Owner: NLM*
* Record type: Completed*
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* 2/3,AB/28*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*00420605 68314188 PMID: 4298110*
* *Thrombocytopenia* in guinea pigs infected by encephalomyocarditis* *virus (EMC).*
* Modai Y; Oren R; De Vries A; Kohn A*
* Thrombosis et diathesis haemorrhagica (GERMANY, WEST) Dec 31 1967, 18* * (3-4) p686-90, ISSN 0340-5338 Journal Code: 7608420* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
*? s gmcsf or gm()csf and platelets*
* 155 GMCSF*
* 25852 GM*
* 43880 CSF*
* 9861 GM(W)CSF*
* 66172 PLATELETS*
* S3 357 GMCSF OR GM()CSF AND PLATELETS*
*? s s3/ti*
* S4 63 S3/TI*
*? t s4/3,ab/all*
**
* 4/3,AB/1*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*14906254 22653709 PMID: 12769449*
* Keeping the M in mind: recombinant human *GMCSF* and Crohn's disease.* * Bickston Stephen J*
* Digestive Health Center of Excellence, University of Virginia,* *Charlottesville, Virginia, USA.*
* Inflammatory bowel diseases (United States) Mar 2003, 9 (2) p132,* *ISSN 1078-0998 Journal Code: 9508162*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: In Process*
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* 4/3,AB/2*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*14810374 22582005 PMID: 12695562*
* Human *platelets* produce granulocyte-macrophage

colony-stimulating* *factor and delay eosinophil apoptosis.*
* Raiden Silvina; Schettini Jorge; Salamone Gabriela; Trevani Analia;* *Vermeulen Monica; Gamberale Romina; Giordano Mirta; Geffner Jorge* * Department of Microbiology, Buenos Aires University School of Medicine,* *Buenos Aires, Argentina.*
* Laboratory investigation; a journal of technical methods and pathology (* *United States) Apr 2003, 83 (4) p589-98, ISSN 0023-6837* *Journal Code: 0376617*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* An association between eosinophils and platelets has been described in* *several diseases, most notably asthma. Although the mechanisms through* *which platelets influence eosinophil behavior are not well defined,* *platelets seem to contribute to the selective accumulation of eosinophils* *at sites of allergic inflammation by virtue of their ability to produce* *eosinophil chemotactic factors. We report here for the first time that* *platelets delay apoptosis, thus enhancing eosinophil survival. A marked* *inhibition of spontaneous apoptosis was observed using eosinophil:platelet* *ratios of 1:50, 1:25, 1:10, and 1:5. Moreover, promotion of eosinophil* *apoptosis by either pronase or dexamethasone was also inhibited greatly in* *the presence of platelets. The antiapoptotic effect mediated by platelets* *was dependent on the release of soluble products and was significantly* *inhibited by neutralizing antibodies directed to GM-CSF. Studies performed* *by flow cytometry, directed to analyze the cellular source of this* *cytokine, demonstrated that intracytoplasmic GM-CSF is present in resting* *platelets. Moreover, GM-CSF was found in platelet supernatants, at* *concentrations able to prevent eosinophil apoptosis. Our findings support a* *novel mechanism through which platelets may contribute to eosinophil* *accumulation at allergic inflammatory sites.* **
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* 4/3,AB/3*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*14801313 22616079 PMID: 12731089*
* Preclinical evaluation of DISC-*GMCSF* for the treatment of breast* *carcinoma.*
* Loudon Peter T; McLean Cornelia S; Martin Gilly; Curry Jayne; Leigh Shaw* *M; Hoogstraten Conny; Verdegaal Els; Osanto Susanne*
* Xenova Group plc, 310 Cambridge Science Park, Cambridge CB4 0WG, UK.* * journal of gene medicine (England) May 2003, 5 (5) p407-16, ISSN* *1099-498X Journal Code: 9815764*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: In Process*
* BACKGROUND: DISC-hGMCSF is a gH-deleted HSV-2 based vector expressing* *human GM-CSF that has entered clinical trials for the therapy of metastatic* *melanoma. To determine whether this product also has potential to treat* *breast carcinoma, a series of in vitro and in vivo studies were made.* *METHODS: Breast carcinoma cell lines and primary cultures of breast* *carcinoma cells were infected with DISC-GFP or DISC-human-GMCSF* *(DISC-hGMCSF) and the number of GFP-positive cells and GM-CSF yields were* *determined. In vivo efficacy of DISC-murine-GMCSF (DISC-mGMCSF) in* *combination with systemic chemotherapy was assessed in the murine 4T1* *breast carcinoma model by direct injection into subcutaneous tumours.* *RESULTS: DISC-hGMCSF was able to infect all breast carcinoma cell lines and* *the majority of primary breast carcinoma cultures with high efficiency,* *although culture-to-culture variability in infectability was noted in the* *latter. In the MCF-7 breast carcinoma cell line, expression of hGMCSF was* *found to peak over the first 24 h post-infection and drop to background* *levels by 7 to 14 days. In the 4T1 murine breast tumour model, injection of* *subcutaneous tumours led to a delay in tumour growth and, in rare cases,* *complete regression of visible tumour. DISC-mGMCSF and DISC-LacZ showed* *similar levels of efficacy. When mice were given simultaneous 5FU* *chemotherapy the effectiveness of DISC-mGMCSF treatment was undiminished,* *and up to three out of ten mice showed complete absence of visible tumour.* *CONCLUSIONS: DISC-hGMCSF is able to infect human breast carcinoma cells at* *high efficiency and express GM-CSF. DISC-mGMCSF demonstrated efficacy in* *the murine 4T1 model, even during concomitant chemotherapy. Taken together* *these results indicate that DISC-hGMCSF may have potential for the* *treatment of breast carcinoma. Copyright 2003 John Wiley & Sons, Ltd.* **
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* 4/3,AB/4*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*13979986 22255231 PMID: 12368687*
* The majority of children and adolescents with acute myeloid leukemia have* *detectable anti-DT388-*GMCSF* IgG concentrations, but at concentrations* *that should not preclude in vivo activity.*
* Hall Philip D; Razzouk Bassem I; Willoughby Tony E; McLean Thomas W;* *Frankel Arthur E; et al*
* Department of Pharmaceutical Sciences, Medical University of South* *Carolina, Charleston 29425,

USA.*
* Journal of pediatric hematology/oncology - official journal of the* *American Society of Pediatric Hematology/Oncology (United States) Oct* *2002, 24 (7) p521-6, ISSN 1077-4114 Journal Code: 9505928* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* PURPOSE: As a novel approach for the treatment of acute myeloid leukemia* *(AML), the authors are developing a fusion toxin (DT(388)-GMCSF) consisting* *of a truncated diphtheria toxin (DT(388)) linked to human* *granulocyte-macrophage colony-stimulating factor (GMCSF). A critical step* *in the development of DT(388)-GMCSF for clinical use in childhood and* *adolescent AML is to determine whether children and adolescents have* *preexisting antibodies to DT(388)-GMCSF due to childhood immunizations* *against diphtheria toxoid. PATIENTS AND METHODS: Sera from 33 children and* *adolescents with AML and one with juvenile myelomonocytic leukemia were* *collected. The median age was 11.8 years. All scheduled diphtheria toxoid* *vaccinations were current except for the child diagnosed at 4 months of* *age. Anti-DT(388)-GMCSF antibody concentrations were detected by an* *enzymoimmunoassay and by an in vitro bioassay. RESULTS: Thirty of 34 (88%)* *children and adolescents had detectable anti-DT(388)-GMCSF IgG antibody* *concentrations. The median concentration was 1.5 microg/mL, with a range* *from undetectable to 191.4 microg/mL. There was a positive correlation* *between the enzymoimmunoassay and bioassay. There was no difference between* *the anti-DT(388)-GMCSF IgG concentrations in these children and adolescents* *with AML and in 43 adults with AML. Preliminary results of the phase 1* *trial of DT -GMCSF in adults with AML indicate that patients with baseline* *anti-DT(388)-GMCSF IgG concentrations of less than 2 microg/mL can achieve* *circulating DT(388)-GMCSF concentrations and can exhibit antileukemic* *activity. Twenty-three of 34 (67.6%) children and adolescents had* *anti-DT(388)-GMCSF IgG concentrations less than 2 microg/mL. CONCLUSIONS:* *Despite routine diphtheria toxoid vaccinations, most children and* *adolescents with AML do not have anti-DT -GMCSF IgG concentrations that* *preclude in vivo activity of DT -GMCSF.*
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* 4/3,AB/5*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*13917987 22122495 PMID: 12132046*
* *GM*-*CSF*-based mobilization effect in normal healthy donors for* *allogeneic peripheral blood stem cell transplantation.* * Sohn S K; Kim J G; Seo K W; Chae Y S; Jung J T; Suh J S; Lee K B; et al* * Department of Hematology/Oncology, Kyungpook National University* *Hospital, 50 Samduck-2ka, Taegu, South Korea, 700-421.* * Bone marrow transplantation (England) Jul 2002, 30 (2) p81-6, ISSN* *0268-3369 Journal Code: 8702459*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: In Process*
* It is important to optimize methods to mobilize hematopoietic stem cells* *into peripheral blood (PB) for successful allogeneic peripheral blood stem* *cell (PBSC) transplantation. Our primary intent was to investigate the role* *of GM-CSF for mobilization in normal healthy donors and to compare its* *efficacy in mobilizing stem cells alone, in concurrent combination and in* *sequential combination with G-CSF in this study. We analyzed the results of* *the PBSC harvest through large volume leukapheresis from 48 normal healthy* *donors mobilized by three different regimens including GM-CSF. Donors were* *assigned sequentially to one of the following regimens for mobilization:* *GM-CSF 10 microg/kg/day alone (group 1, n = 9); concurrent combination* *(group 2, n = 20) of G-CSF 5 microg/kg/day and GM-CSF 5 microg/kg/day;* *sequential combination (group 3, n = 19) of GM-CSF alone 10 microg/kg/day* *for 3 days followed by G-CSF alone 10 microg/kg/day for 2-3 days. The* *harvested CD34(+) cell count (P < 0.05) was statistically higher in group 3* *than in group 1 or 2. Pre-collection WBC count in donors (P < 0.05),* *harvested MNC (P < 0.05) and CD3(+) cell count (P < 0.05) of group 2 or 3* *were significantly higher than those of group 1. Recipients who received* *stem cells mobilized with combination regimens showed an earlier recovery* *of WBC and platelets count than those with GM-CSF alone. The incidence of* *acute graft-versus-host disease was not statistically different among three* *recipient groups. GM-CSF-based mobilization was well tolerated in normal* *healthy donors. The sequential combination regimen appears to be an* *excellent mobilization strategy and might be preferred as the optimal* *method in some clinical situations that need a higher number of stem cells.* **
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* 4/3,AB/6*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11899022 99341877 PMID: 10414911*
* Hematopoietic growth factor after autologous peripheral blood* *transplantation: comparison of G-CSF and *GM*-*CSF*.* * Jansen J; Thompson E M; Hanks S; Greenspan A R; Thompson J M; Dugan M J;* *Akard L P*
* Indiana Blood and Marrow Transplantation, Indianapolis

46202, USA.* * Bone marrow transplantation (ENGLAND) Jun 1999, 23 (12) p1251-6,* *ISSN 0268-3369 Journal Code: 8702459*
* Document type: Clinical Trial; Controlled Clinical Trial; Journal Article* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Autologous peripheral blood stem cell (PBSC) transplantation results in* *rapid hematologic recovery when sufficient numbers of CD34+ cells/kg are* *infused. Recent studies suggest that filgrastim (G-CSF) administration* *following transplantation leads to more rapid neutrophil recovery and lower* *total transplant costs. This study compares the use of G-CSF (5* *microg/kg/day) with sargramostim (GM-CSF) 500 microg/day from day 0 until* *neutrophil recovery (ANC >1500/mm3) in patients with breast cancer or* *myeloma who had PBSC mobilized with the combination of cyclophosphamide,* *etoposide, and G-CSF. Twenty patients (13 breast cancer and seven myeloma)* *received GM-CSF and 26 patients (14 breast cancer and 12 myeloma) received* *G-CSF. The patients were comparable for age and stage of disease, and* *received stem cell grafts that were not significantly different (CD34+ x* *10(6)/kg was 12.5 +/- 11.1 (mean +/- s.d.) for GM-CSF and 19.8 +/- 18.5 for* *G-CSF; P = 0.10). The use of red cells (2.8 vs 2.3 units), and platelet* *transfusions (2.5 vs 3.1) was similar for the two groups, as was the use of* *intravenous antibiotics (4.3 vs 4.6 days) and the number of days with* *temperature >38.3 degrees C (2.3 vs 1.8). Platelet recovery was also* *similar in both groups (platelets >50,000/mm3 reached after 11.8 vs 14.9* *days). The recovery of neutrophils, however, was faster using G-CSF. ANC* *>500/mm3 and >1000/mm3 were reached in the GM-CSF group at 10.5 +/- 1.5 and* *11.0 +/- 1.7 days, respectively, whereas with G-CSF only 8.8 +/- 1.2 and* *8.9 +/- 2.2 days were required (P < 0.001). As a result, patients given* *G-CSF received fewer injections than the GM-CSF patients (10.9 vs 12.3).* *Resource utilization immediately attributable to the use of growth factors* *and the duration of pancytopenia, excluding hospitalization, were similar* *for the two groups. This study suggests that neutrophil recovery occurs* *more quickly following autologous PBSC transplant using G-CSF in comparison* *to GM-CSF, but the difference is not extensive enough to result in lower* *total cost.*
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* 4/3,AB/7*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11893819 99336323 PMID: 10407985*
* Colony stimulating factors in polychemotherapy of testicular tumors. A* *comparison between G-CSF and *GM*-*CSF*]*
* Koloniestimulierende Faktoren bei der Polychemotherapie von Hodentumoren.* *Ein Vergleich zwischen G-CSF und *GM*-*CSF*.* * Will R; Hofmockel G; Langer W; Frohmuller H*
* Urologische Klinik und Poliklinik, Universitat Wurzburg.* * Der Urologe. Ausg. A (GERMANY) May 1999, 38 (3) p258-63, ISSN* *0340-2592 Journal Code: 1304110*
* Document type: Journal Article ; English Abstract*
* Languages: GERMAN*
* Main Citation Owner: NLM*
* Record type: Completed*
* Colony-stimulating factors (CSF) are frequently used in cases of* *cytostatic therapy of patients with testicular cancer assuming that they* *support hematopoietic recovery and, thus, shorten duration of neutropenia* *as well as reduce infections. Currently, G-CSF and GM-CSF are clinically* *used. In the present study efficacy and toxicity of these two drugs were* *investigated and compared in patients with testicular cancer treated by* *standard chemotherapy. Studying 83 chemotherapy cycles applied to 31* *patients with advanced germ cell tumors the effectivity and the side* *effects of the two CSF were examined by questioning, clinical evaluation,* *and blood chemistry studies. G-CSF (480 micrograms subcutaneously (s.c.))* *were used in 55 and GM-CSF (400 micrograms s.c.) in 28 chemotherapeutic* *cycles. The indications consisted in the treatment of leukocytopenia on the* *one hand and in the prophylaxis in subsequent cycles on the other hand. No* *difference between the two CSF could be found either with regard to* *postponement of the next cycle (G-CSF: 6.8 vs. GM-CSF: 7.3 days), or to the* *number of injections per cycle (G-CSF: 8 vs. GM-CSF: 12.5), or to the* *leukocyte (G-CSF: 2.1 vs. GM-CSF: 1.6 x 10(3)/microliter) or platelet nadir* *(G-CSF: 0.5 vs. GM-CSF: 0.5 x 10(5)/microliter; mean values of all cycles,* *respectively). Both CSF did not seem to influence the production of* *platelets. However, a difference between the two CSF was demonstrated with* *respect to the toxicity. Frequency (G-CSF: 38.5% vs. GM-CSF: 69.3%) as well* *as intensity of side effects causing a change of the drug (G-CSF: n = 1 vs.* *GM-CSF: n = 7) were lower in the case of G-CSF. In conclusion, these data* *demonstrate no difference was seen between G-CSF and GM-CSF with respect to* *the efficacy in patients with testicular cancer treated by standard* *chemotherapy. However, the use of G-CSF seems to be associated with lower* *toxicity.*
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* 4/3,AB/8*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11788070 99226735 PMID: 10211753*
* G-CSF versus *GM*-*CSF* for stimulation of

peripheral blood* *progenitor cells (PBPC) and leukocytes in healthy volunteers: comparison of* *efficacy and tolerability.*
* Fischmeister G; Kurz M; Haas O A; Micksche M; Buchinger P; Printz D;* *Ressmann G; Stroebel T; Peters C; Fritsch G; Gadner H* * Children's Cancer Research Institute, St. Anna Kinderspital, Vienna,* *Austria.*
* Annals of hematology (GERMANY) Mar 1999, 78 (3) p117-23, ISSN* *0939-5555 Journal Code: 9107334*
* Document type: Clinical Trial; Journal Article; Randomized Controlled* *Trial*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* This study compared two recombinant human (rh) hematopoietic growth* *factors in healthy volunteers for stem cell stimulation. Granulocyte* *colony-stimulating factor (G-CSF, n=9) or granulocyte-macrophage* *colony-stimulating factor (GM-CSF, n=8) was given subcutaneously for 5 days* *(5 microg/kg/day). Controls (n=5) received no growth factor. Laboratory* *parameters and side effects were monitored for 8 days. Within 24 h, both* *cytokines led to a rapid increase of leukocytes, the majority of which were* *granulocytes. Compared with the controls (n=5), the increase on day 5 in* *the G-CSF/GM-CSF groups was 37-/10-fold (CD34+ cells), 5.2-/2.4-fold* *(leukocytes), 7.2-/3.0-fold (granulocytes), 7.4-/4.4-fold (monocytes),* *1.7-/1.1-fold (lymphocytes), 9.8-/2.7-fold (basophils), 2.3-/9.6-fold* *(eosinophils), and 1.9-/1.6-fold (reticulocytes). The mobilization of* *myeloblasts, promyelocytes, myelocytes, and metamyelocytes coincided with* *the pronounced increase of CD34 + PBPC observed on day 4. Serum levels of* *uric acid (UA) and lactic dehydrogenase (LDH) increased under G-CSF, and* *platelets decreased after G-CSF discontinuation. Rash at the injection site* *occurred in 50% of the GM-CSF-treated volunteers. Seven volunteers in the* *GM-CSF group and six in the G-CSF cohort complained of flu-like symptoms,* *including musculoskeletal pain. We conclude that, in terms of tolerance and* *mobilization of CD34+ cells and leukocytes, G-CSF is superior to GM-CSF,* *but higher levels of UA and LDH and late decrease in platelets make* *monitoring of these parameters necessary.*
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* 4/3,AB/9*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11718151 99154616 PMID: 10037012*
* Long-term treatment with *GM*-*CSF* in patients with chronic* *lymphocytic leukemia and recurrent neutropenic infections.* * Itala M; Pelliniemi T T; Remes K; Vanhatalo S; Vainio O* * Turku University Central Hospital, Dept. of Medicine, Finland.* * Leukemia & lymphoma (SWITZERLAND) Dec 1998, 32 (1-2) p165-74, ISSN* *1042-8194 Journal Code: 9007422*
* Document type: Clinical Trial; Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* In this prospective study we evaluated the multiple effects of long-term* *GM-CSF therapy on blood counts, granulocyte functions and disease* *progression in patients with chronic lymphocytic leukemia (CLL) with* *chronic neutropenia and recurrent bacterial infections. The treatment* *duration varied from 2 to 12 weeks. The neutrophil count was raised in all* *patients, by the median of 6.6-fold. The neutrophil level of 1.0 x 10(9)/l* *was usually reached after two weeks. The initial dose of GM-CSF was 5* *microg/kg/day, and 1-7 microg/kg/day was required to maintain the* *neutrophil level above 1.0 x 10(9)/l. Granulocyte functions, i.e.* *chemiluminescence (CL), random migration, and fMLP-stimulated chemotaxis* *were initially depressed in all patients when compared to healthy controls.* *GM-CSF enhanced significantly CL even when given at small doses (less than* *1 microg/kg/day), even lower than the dose required to promote* *granulopoiesis. We conclude that GM-CSF is effective in improving CLL* *associated chronic neutropenia and also enhances impaired granulocyte* *chemiluminescence. Thus, GM-CSF could be helpful for giving chemotherapy* *without neutropenic delays and for prophylaxis of infectious complications* *in CLL patients.*
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* 4/3,AB/10*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11628292 99061782 PMID: 9845531*
* Thrombopoietin induces association of Crkl with STAT5 but not STAT3 in* *human *platelets*.*
* Ozaki K; Oda A; Wakao H; Rhodes J; Druker B J; Ishida A; Wakui M; Okamoto* *S; Morita K; Handa M; Komatsu N; Ohashi H; Miyajima A; Ikeda Y* * Division of Hematology, Department of Internal Medicine, and Blood* *Center, Keio University, Tokyo, Japan.*
* Blood (UNITED STATES) Dec 15 1998, 92 (12) p4652-62, ISSN 0006-4971* *Journal Code: 7603509*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Crkl, a 39-kD SH2, SH3 domain-containing adapter protein, is* *constitutively tyrosine phosphorylated in hematopoietic cells from chronic*

*myelogenous leukemia (CML) patients. We recently reported that* *thrombopoietin induces tyrosine phosphorylation of Crkl in normal* *platelets. In this study, we demonstrate that thrombopoietin induces* *association of Crkl with a tyrosine phosphorylated 95- to 100-kD protein in* *platelets and in UT7/TPO cells, a thrombopoietin-dependent megakaryocytic* *cell line. With specific antibodies against STAT5, we demonstrate that the* *95- to 100-kD protein in Crkl immunoprecipitates is STAT5. This* *coimmunoprecipitation was specific in that Crkl immunoprecipitates do not* *contain STAT3, although STAT3 becomes tyrosine phosphorylated in* *thrombopoietin-stimulated platelets. The coimmunoprecipitaion of Crkl with* *STAT5 was inhibited by the immunizing peptide for Crkl antisera or phenyl* *phosphate (20 mmol/L). After denaturing of Crkl immunoprecipitates, Crkl* *was still immunoprecipitated by Crkl antisera. However,* *coimmunoprecipitation of STAT5 was not observed. Coincident with STAT5* *tyrosine phosphorylation, thrombopoietin induces activation of STAT5* *DNA-binding activity as demonstrated by electrophoretic mobility shift* *assays (EMSA). Using a beta-casein promoter STAT5 binding site as a probe,* *we have also demonstrated that Crkl antisera supershift the STAT5-DNA* *complex, suggesting that Crkl is a component of the complex in the nucleus.* *Furthermore, interleukin-3 (IL-3), granulocyte-macrophage colony-stimulatin* *g factor (GM-CSF), and erythropoietin also induce Crkl-STAT5 complex* *formation in responding cells in a stimulation-dependent manner. In vitro,* *glutathione S-transferase (GST)-Crkl bound to STAT5 inducibly through its* *SH2 domain. These results indicate that thrombopoietin, IL-3, GM-CSF, and* *erythropoietin commonly induce association of STAT5 and Crkl and that the* *complex translocates to the nucleus and binds to DNA. Interestingly, such* *association between STAT5 and Crkl was not observed in cytokine-stimulated* *murine cells, suggesting an intriguing possibility that components of the* *human STAT5-DNA complex may be different from those of the murine* *counterpart.*
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* 4/3,AB/11*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11616110 99049172 PMID: 9832332*
* Regulation of interleukin-1-stimulated *GMCSF* mRNA levels in human* *endothelium.*
* Patterson C E; Stasek J E; Bahler C; Verin A D; Harrington M A; Garcia J* *G*
* Department of Medicine and the Walther Oncology Center, Indiana* *University School of Medicine, Richard L. Roudebush Veteran's* *Administration Center, Indianapolis 46202, USA.*
* Endothelium - journal of endothelial cell research (SWITZERLAND) 1998,* * 6 (1) p45-59, ISSN 1062-3329 Journal Code: 9412590* * Contract/Grant No.: GM43972; GM; NIGMS; HL 57462; HL; NHLBI; HL50533; HL;* *NHLBI*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The regulation of interleukin-1 (IL-1)-mediated increases in GMCSF mRNA* *levels in human endothelium was examined and determined to occur in a time-* *and protein kinase C (PKC)-dependent manner. IL-1beta induced the early* *activation and translocation of PKC isotypes alpha and beta2 to the nucleus* *and PKC inhibition attenuated the IL-1-mediated increase in GMCSF mRNA* *levels. PKC activation by PMA alone, in the absence of IL-1beta activation,* *however, was insufficient to allow GMCSF mRNA detection. Increasing cyclic* *adenosine nucleotide (cAMP) levels suppressed IL-1beta-induced increases in* *GMCSF mRNA levels. In contrast, botulinum toxin C, which mediates the ADP* *ribosylation of a 21 kD ras-related G protein, augmented IL-1beta-induced* *GMCSF mRNA expression. Inhibition of protein synthesis (with cycloheximide)* *raised basal GMCSF mRNA transcripts to detectable levels, augmented* *IL-1-induced increases in GMCSF mRNA levels, and exhibited negative* *regulation by cAMP. Finally, disruption of either microtubules (with* *colchicine) or microfilaments (with cytochalasin B) resulted in reduced* *GMCSF mRNA expression in response to IL-1beta. These results are compatible* *with a model wherein IL-1-mediated increases in human endothelial cell* *GMCSF mRNA may be linked to both nuclear protein kinase C activation and* *activation of a low molecular weight G-protein, although neither activity* *alone is sufficient to increase the levels of GMCSF mRNA.* **
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* 4/3,AB/12*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11491590 98375734 PMID: 9711916*
* Anti-*GM*-*CSF* monoclonal antibody therapy for refractory acute* *leukemia.*
* Bouabdallah R; Olive D; Meyer P; Lopez M; Sainty D; Hirn M; Mannoni P;* *Fougereau E; Gastaut J A; Maraninchi D*
* Department of Haematology, Institut Paoli-Calmettes, Marseille, France.* * Leukemia & lymphoma (SWITZERLAND) Aug 1998, 30 (5-6) p539-49, ISSN* *1042-8194 Journal Code: 9007422*
* Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article* * Languages: ENGLISH*

* Main Citation Owner: NLM*
* Record type: Completed*
* Several phase I trials and pilot studies using Monoclonal Antibody (MoAb)* *have been performed in B-cell neoplasms, but this approach has not until* *now been extensively tested in myeloid leukemias. Recently, we evaluated* *the use of anti-Granulocyte-Macrophage Colony-Stimulating Factor MoAb* *(Anti-GM-CSF MoAb) in acute myeloid leukemia (AML). Eight patients* *fulfilled inclusion criteria and received a single course of Anti-GM-CSF* *MoAb infusion during 5 to 15 days. Anti-GM-CSF MoAb was well tolerated and* *was detectable in pharmacokinetics studies. Using Human Anti-Rat Antibodies* *(HARA), we also observed an immunological response to the MoAb. Despite* *sufficient levels detected in the serum and biological activity of* *Anti-GM-CSF MoAb in vivo, no anti-leukemic effect was noted, except for one* *patient who had a decrease of 50% in the marrow blast cell mass. These* *observations indicate that leukemic proliferation in vivo involves a* *complex network spanning many mechanisms, and inhibition of leukemia is not* *effective if only one of these key targets is attacked. The development of* *these new approaches may be more effective in the future.* **
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* 4/3,AB/13*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11459003 98342267 PMID: 9675065*
* Production of recombinant DTctGMCSF fusion toxin in a baculovirus* *expression vector system for biotherapy of *GMCSF*-receptor positive* *hematologic malignancies.*
* Williams M D; Rostovtsev A; Narla R K; Uckun F M*
* Department of Protein Engineering, Alexander Parker Pharmaceuticals,* *Inc., Roseville, Minnesota, 55113, USA.*
* Protein expression and purification (UNITED STATES) Jul 1998, 13 (2)* * p210-21, ISSN 1046-5928 Journal Code: 9101496*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The fusion toxin DTctGMCSF has been constructed by genetically replacing* *the native receptor-binding domain of diphtheria toxin (DT) with human* *granulocyte-macrophage colony stimulating factor (GMCSF). This recombinant* *fusion toxin preserves the catalytic (c) and membrane translocation (t)* *domains of DT and includes a sterically neutral peptide linker separating* *the toxin and growth factor domains. Previous work using DTctGMCSF produced* *in Escherichia coli has shown that this chimeric toxin is selectively* *cytotoxic to GMCSF receptor (R)-positive acute myeloid leukemia (AML) cells* *both in vitro and in vivo. Its clinical development has been hampered due* *to very low expression levels, requirements for solubilization with* *guanidine hydrochloride and subsequent refolding, and concerns about* *bacterial endotoxin contamination. These difficulties prompted us to* *investigate the utility of a baculovirus/insect cell expression system for* *the production of DTctGMCSF. Here, we report that a soluble form of* *DTctGMCSF can be produced in the baculovirus expression vector system* *(BEVS) and purified to homogeneity by column chromatography. The* *BEVS-derived DTctGMCSF fusion toxin caused apoptotic death in* *GMCSF-R-positive human AML cells at nanomolar concentrations. In contrast* *to the 100 microg/L yields of purified DTctGMCSF obtained from E. coli, the* *BEVS allows us to routinely generate 8-10 mg/L of purified DTctGMCSF. This* *increased capacity provided by the BEVS for the production of DTctGMCSF* *makes it now possible to obtain sufficient quantities to carry out* *preclinical and clinical trials. To our knowledge, this is the first report* *of the successful utilization of the BEVS for producing a therapeutic* *fusion toxin. Copyright 1998 Academic Press.*
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* 4/3,AB/14*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11451306 98334519 PMID: 9667951*
* Cell-specific modulation of drug resistance in acute myeloid leukemic* *blasts by diphtheria fusion toxin, DT388-*GMCSF*.* * Frankel A E; Hall P D; McLain C; Safa A R; Tagge E P; Kreitman R J* * Department of Medicine, Medical University of South Carolina, Charleston,* *South Carolina 29425, USA.*
* Bioconjugate chemistry (UNITED STATES) Jul-Aug 1998, 9 (4) p490-6,* *ISSN 1043-1802 Journal Code: 9010319*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Radiochemotherapy-resistant blasts commonly cause treatment failure in* *acute myeloid leukemia (AML), and their resistance is due, in part, to* *overexpression of multidrug resistance (mdr) proteins. We reasoned that* *targeted delivery of protein synthesis inactivating toxins to leukemic* *blasts would reduce the cellular concentrations of relatively short* *half-life resistance proteins and sensitize the cells to cytotoxic drugs.* *To test this hypothesis, we employed human granulocyte-macrophage* *colony-stimulating factor fused to truncated diphtheria toxin* *(DT388-GMCSF). The human AML

cell line HL60 and its vincristine-resistant* *sublines, HL60Vinc and HL60VCR, were incubated in vitro for 24 h with* *varying concentrations of toxin. Doxorubicin was added for an additional 24* *h, and cell cytotoxicity was assayed by thymidine incorporation and colony* *formation in semisolid medium. DT388-GMCSF sensitized HL60Vinc and HL60VCR* *but not HL60 to doxorubicin. Combination indices for three log cell kill* *varied from 0.2 to 0.3. In contrast, pretreatment with doxorubicin followed* *by toxins failed to show synergy. At least in the case of the* *vincristine-resistant cell lines, modulation of drug resistance correlated* *with reduction in membrane P-glycoprotein concentrations based on* *immunoblots with C219 antibody, flow cytometry with MRK16 antibody, and* *cell uptake of doxorubicin. These observations suggest clinical trials of* *combination therapy may be warranted in patients with refractory AML.* *Further, targeted toxins may represent a novel class of cell-specific* *modulators of drug resistance for a number of malignancies.* **
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* 4/3,AB/15*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11282229 98160808 PMID: 9499829*
* Characterization of peripheral blood steady-state progenitor cells* *preserved in liquid culture conditions with or without *GM*-*CSF** * and IL2.*
* Sawadogo D; Martinez M J; Merino J; Subira M L; Brugarolas A* * Department of Oncology, Facultad de Medicina, Universidad de Navarra,* *Pamplona, Spain.*
* Revista de medicina de la Universidad de Navarra (SPAIN) Oct-Dec 1996,* * 40 (4) p7-14, ISSN 0556-6177 Journal Code: 0123071* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The cellular characteristics of steady-state peripheral blood progenitor* *cell (PBPC) apheresis, including total number of lymphomononuclear cells,* *CD34 and CFUs, was evaluated in a group of 26 chemo-radiotherapy patients* *as well as in a group of 23 surgically resected cancer patients. Three-to* *seven-day incubation in standard liquid culture conditions with growth* *factors (IL2, GM-CSF or both) correlated with a statistically significant* *increase in CD34+ and CD56+ cell populations compared with incubation* *without growth factors, especially when both GM-CSF and IL2 were used. In* *addition, an increase in CD33+, CD13+ and HLA-DR+ cell populations was* *observed after 3-7 days incubation with GM-CSF. The basal culture control* *exhibited a decrease in CD33+ and CD13+ cell populations while CD34+ and* *CD56+ cell populations were maintained. These results were similar in the* *treated and untreated groups of patients. The infusion of GM-CSF and IL2* *preincubated PBPC after intensive chemotherapy was associated with a rapid* *hematological recovery with a median time duration for WBC < 500/uL, WBC <* *1.000/uL and platelets < 20.000/uL of 7.9 days, 14.9 days and 10.7 days* *respectively. We conclude that a short GM-CSF and IL2 preincubation of* *steady-state PBPC is associated with an increase in cell populations* *exhibiting the immune and progenitor cell phenotypes and correlates with an* *early hematological recovery after intensive chemotherapy.* **
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* 4/3,AB/16*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11251481 98129052 PMID: 9467871*
* The effect of uteroferrin and recombinant *GM*-*CSF* on* *hematopoietic parameters in normal female pigs (Sus scrofa).* * Laurenz J C; Hadjisavas M; Schuster D; Bazer F W*
* Department of Animal Science, Texas A&M University, College Station* *77843-2471, USA.*
* Comparative biochemistry and physiology. Part B, Biochemistry & molecular* *biology (ENGLAND) Nov 1997, 118 (3) p579-86, ISSN 1096-4959* *Journal Code: 9516061*
* Contract/Grant No.: DK 46766; DK; NIDDK*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The present study investigated the effect of uteroferrin and recombinant* *bovine granulocyte-monocyte/macrophage colony stimulating factor (rbGM-CSF)* *on hematopoiesis in young female pigs. Uteroferrin (100 micrograms/kg in* *0.9% NaCl), rbGM-CSF (10 micrograms/kg in 0.9% NaCl), uteroferrin +* *rbGM-CSF (as above), or control (0.9% NaCl) were administered as* *intramuscular injections twice daily (0800 and 2000 hr). Peripheral blood* *cell number, composition, and progenitor cells were determined over 28* *days. Uteroferrin had minimal effects on white blood cell (WBC) number,* *while rbGM-CSF caused both a rapid (days 2-7; maximum 122 +/- 8% of* *baseline) and late (days 16-28; maximum 133 +/- 8% of baseline) increase in* *WBC. Combination treatment with uteroferrin + rbGM-CSF abolished the* *initial increase in WBC number,but resulted in a prolonged increase in WBC* *number (days 14-28) relative to control. The rbGM-CSF-induced increase in* *WBC number resulted from rapid increases (P < 0.05) in monocytes and* *neutrophils. The addition of uteroferrin + rbGM-CSF enhanced (P < 0.05) the* *initial increase in the monocyte population and augmented the neutrophilia.* *In addition, uteroferrin +

rbGM-CSF resulted in a dramatic eosinophilia* *(days 2-28), which was not detected in either the uteroferrin or rbGM-CSF* *treatments. Although not substantially affected by uteroferrin alone,* *rbGM-CSF caused an increase (P < 0.05) in thrombocyte numbers from days 1* *through 9 (maximum 133 +/- 11% of baseline), an effect augmented by* *cotreatment with uteroferrin. The ability of these cytokines to modulate* *blood cell number and composition appeared to result from their effects on* *hematopoietic progenitor cells. Treatment of pigs with uteroferrin* *increased (P < 0.05) CFU-GEMM, CFU-GM, and BFU-E progenitor cells in* *peripheral blood, while rbGM-CSF caused increases (P < 0.05) relative to* *control in CFU-GM and CFU-GEMM. These effects were additive, as uteroferrin* *+ GM-CSF augmented the increases in CFU-GM, BFU-E, and CFU-GEMM.* *Collectively, these results indicate that uteroferrin and rbGM-CSF can* *modulate hematopoiesis in young pigs. These effects were both additive and,* *in the case of neutrophils and eosinophils, synergistic. Hence, the* *mechanism(s) by which uteroferrin and rbGM-CSF modulate hematopoiesis* *appear to be different.*

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* 4/3,AB/17*

*DIALOG(R)File 155:MEDLINE(R)*

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*11251480 98129051 PMID: 9467870*

* Uteroferrin and recombinant bovine *GM*-*CSF* modulate the* *myelosuppressive effects of 5-fluorouracil in young female pigs (Sus* *scrofa).*

* Laurenz J C; Hadjisavas M; Schuster D; Bazer F W*

* Department of Animal Science, Texas A&M University, College Station* *77843-2471, USA.*

* Comparative biochemistry and physiology. Part B, Biochemistry & molecular* *biology (ENGLAND) Nov 1997, 118 (3) p569-77, ISSN 1096-4959* *Journal Code: 9516061*

* Contract/Grant No.: DK 46766; DK; NIDDK*

* Document type: Journal Article*

* Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* The present study investigated the ability of uteroferrin and recombinant* *bovine granulocyte monocyte/macrophage-colony stimulating factor (rbGM-CSF)* *to modulate the myelosuppressive effects of 5-fluorouracil (5-FU) in young* *female pigs (Sus scrofa). Pigs (N = 3/treatment) were infused with 5-FU* *(32.5 mg/kg) on days 0 and 1 of the experimental period. Uteroferrin (100* *micrograms/kg in 0.9% NaCl), rbGM-CSF (10 micrograms/kg in 0.9% NaCl),* *uteroferrin + rbGM-CSF (as above) or control (0.9% NaCl) were administered* *as intramuscular injections twice daily (0800 and 2000 hr). Peripheral* *blood cell number, composition, and progenitor cells were determined over* *28 days. Treatment of pigs resulted in a rapid leukocytopenia and* *thrombocytopenia (nadirs on days 5 and 7, respectively) and a modest* *decrease (P < 0.05) in red blood cell (RBC) number (nadir on day 14).* *Although nor affecting RBC and thrombocytes, treatment of pigs with* *uteroferrin had an initial protective effect (P < 0.05) on the 5-FU-induced* *leukocytopenia (63 and 64 vs 48 and 39 +/- 6% of baseline on days 3 and 5,* *respectively). In contrast, rbGM-CSF enhanced (P < 0.05) the rate of the* *leukocytopenia and had only minor effects on thrombocyte numbers relative* *to controls. These effects appeared to be additive, as pigs treated with* *uteroferrin + rbGM-CSF had a reduced rate of leukocytopenia compared to* *pigs treated with rbGM-CSF alone. Uteroferrin + rbGM-CSF also attenuated (P* *< 0.05) the suppression and enhanced (P < 0.05) recovery of RBC and* *thrombocyte numbers following 5-FU treatment. In control pigs, a modest* *rebound leukocytosis (122 +/- 6% of baseline) and thrombocytosis (141 +/-* *9% of baseline) was evident. Uteroferrin enhanced (P < 0.05) the rebound* *leukocytosis (135 +/- 6% of baseline), but attenuated (P < 0.05) the* *thrombocytosis. In contrast, rbGM-CSF enhanced (P < 0.05) the duration of* *the leukocytosis during the recovery phase, an effect augmented by the* *combination of uteroferrin + rbGM-CSF. In addition, treatment with* *uteroferrin + rbGM-CSF resulted in a sustained thrombocytosis (days 12 to* *21). As indicated by changes in CFU-GM, BFU-E, and CFU-GEMM progenitor* *cells in peripheral blood, the effects of uteroferrin and rbGM-CSF appeared* *to reflect their ability to enhance the proliferation and/or* *differentiation of both similar and distinct hematopoietic progenitor* *cells.*

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* 4/3,AB/18*

*DIALOG(R)File 155:MEDLINE(R)*

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*10991407 97344609 PMID: 9200991*

* S-HAM induction chemotherapy with or without *GM*-*CSF* in* *patients with high-risk myelodysplastic syndromes.*

* Verbeek W; Wormann B; Koch P; Aul C; Hinrichs H; Balleisen L; Rowe J M;* *Bennett J; Buchner T; Hiddemann W*

* Department of Hematology/Oncology, Georg-August University, Gottingen,* *Germany.*

* Annals of hematology (GERMANY) May 1997, 74 (5) p205-8, ISSN* *0939-5555 Journal Code: 9107334*

* Document type: Clinical Trial; Journal Article; Multicenter Study;* *Randomized Controlled Trial*

* Languages: ENGLISH*

* Main Citation Owner: NLM*
* Record type: Completed*
* Thirty-one adult patients with high-risk myelodysplastic syndromes (MDS)* *were enrolled in a prospective randomized double-blind placebo-controlled* *trial evaluating the efficacy of sequential high-dose Ara C/mitoxantrone* *chemotherapy with or without GM-CSF. GM-CSF or placebo was given* *subcutaneously once daily at a dose of 250 micrograms/m2 starting 48 h* *prior to chemotherapy and continued until neutrophil recovery. This design* *allowed us to investigate the role of GM-CSF as a priming factor for the* *leukemic clone, as well as its effect on the recovery of normal* *hematopoiesis. Twenty-eight patients are currently evaluable for response.* *The patients reached a complete remission (36%), eight patients had* *persistent MDS (29%), and ten patients died within 6 weeks after the onset* *of treatment (early death). Infectious complications during cytopenia were* *the major cause of death (8/10). Median time to complete hematologic* *recovery (neutrophils > 500/microliter and platelets 20,000/microliter) and* *time to neutrophil recovery above 1500/microliter was 29 and 35 days,* *respectively. Median remission duration was 190 days (6.4 months). Analysis* *of prognostic subgroups showed a low CR rate (25%) and a high early-death* *rate (44%) in patients > 55 years of age, suggesting that the intensified* *treatment approach should be limited to younger patients. No data* *concerning the influence of GM-CSF on response to chemotherapy or duration* *of neutropenia are presently available.*
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* 4/3,AB/19*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*10862301 97213766 PMID: 9060455*
* Sequential potentiation and inhibition of PMN reactivity by maximally* *stimulated *platelets*.*
* Aziz K A; Cawley J C; Treweeke A T; Zuzel M*
* Department of Haematology, The University of Liverpool, United Kingdom.* * Journal of leukocyte biology (UNITED STATES) Mar 1997, 61 (3) p322-8* *, ISSN 0741-5400 Journal Code: 8405628*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* In a recent study, we showed that granulocyte-macrophage* *colony-stimulating factor (GM-CSF) and supernatants from partially* *stimulated platelets undergoing selective alpha-granule release* *synergistically enhanced polymorphonuclear leukocyte (PMN) response to* *N-formyl-methionyl-leucyl-phenylalanine (fMLP). The active factor released* *from platelet alpha-granules was identified as platelet factor four (PF4).* *In this study we investigate the joint effect on PMN reactivity of GM-CSF* *and supernatants from platelets maximally stimulated to release both alpha-* *and dense granule contents. These platelet supernatants enhanced PMN* *chemiluminescence (CL; a measure of the oxidative burst) during short* *incubations, whereas longer incubations led to the loss of this enhancement* *and the prevention of PMN priming by GM-CSF. The platelet-derived* *inhibitory factor was of low molecular weight, originated from the dense* *granule precursor(s), and its generation required the presence of PMN. When* *ATP/ADP were incubated with PMN at concentrations found in platelet-dense* *granules, they produced a similar biphasic effect on PMN reactivity (a* *potentiation followed by inhibition) as seen with the platelet* *supernatants. The inhibitory effect of these nucleotides coincided with* *their conversion to AMP. AMP per se had an immediate inhibitory effect on* *PMN response to fMLP and prevented PMN priming by GM-CSF. This study* *confirms that partially stimulated platelets enhance PMN reactivity.* *However, during maximal stimulation, nucleotides released from the* *platelet-dense granules are converted to AMP, which in turn can counteract* *the PMN priming effects of factors such as PF4 and GM-CSF.* **
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* 4/3,AB/20*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*10842843 97194122 PMID: 9041700*
* Ultrastructure of resting and rh-*GMCSF*-treated human macrophages* *derived from blood monocytes.*
* el Shewemi S; al-Shammary F; al-Zamel F; Soliman R* * Department of Clinical Laboratory Sciences, College of Applied Medical* *Sciences, King Saud University, Riyadh, Kingdom of Saudi Arabia.* * Journal of electron microscopy (JAPAN) Oct 1996, 45 (5) p388-94,* *ISSN 0022-0744 Journal Code: 7611157*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The ultrastructure of cultured blood monocyte-derived human macrophages* *was investigated and correlated under the effect of different doses of* *rh-GMCSF (dose 1 = 25 IU/ml, dose 2 = 125 IU/ml and dose 3 = 250 IU/ml).* *Resting macrophages showed irregular cell borders and pseudopodia pushed* *out in all directions. Their cytoplasm depicted rough endoplasmic reticulum* *and Golgi complex in the perinuclear area. Lipid globules, primary* *lysosomes and mitochondria were characteristically prominent.*
*rh-GMCSF-stimulated macrophages were more

voluminous and their nuclei were* *irregular in outline, with predominance of euochromatin over* *heterochromatin. The cytoplasm was overcrowded by an increasing number of* *organelles including lysosomes, phagolysosomes and mitochondria. Golgi* *complex demonstrated a wide-spread distribution along the cells, with* *profound membrane expansion and cisternal dilatation; especially, in cells* *treated with dose 2. Electron dense osmiophilic deposits (collapsed* *membranes) were seen in association with lipid globules, which were* *commonly polarized at cell peripheries. Most of these changes were dose* *dependent. However, cells treated with dose 3 manifested additionally* *well-developed centrioles, inapparent nuclear membrane, display of* *microfilaments and well-established adhesions. The demonstrated* *ultrastructural changes in rh-GMCSF-treated human macrophages indicated* *pronounced activation, which supports the reported clinical effect of this* *cytokine.*
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* 4/3,AB/21*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*10505150 96315746 PMID: 8724299*
* Prostaglandin E2 enhances interleukin 8 (IL-8) and IL-6 but inhibits* **GMCSF* production by IL-1 stimulated human synovial fibroblasts in* *vitro.*
* Agro A; Langdon C; Smith F; Richards C D*
* Department of Pathology, McMaster University, Hamilton, Ontario, Canada.* * Journal of rheumatology (CANADA) May 1996, 23 (5) p862-8, ISSN* *0315-162X Journal Code: 7501984*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* OBJECTIVE. To examine in vitro the effect of prostaglandin E2 (PGE2) on* *synovial cell cytokine production. METHODS. Human synovial fibroblasts were* *stimulated with PGE2 alone or PGE2 in combination with interleukin 1 alpha* *(IL-1 alpha) (5 ng/ml) and/or indomethacin (10(6) M) and assessed for the* *production of IL-8, IL-6, and granulocyte macrophage colony stimulating* *factor (GMCSF) at the protein and messenger RNA (mRNA) levels. RESULTS.* *PGE2 alone had little detectable effect on IL-8 or GMCSF; however, a small* *enhancement of both IL-6 mRNA and protein levels was seen. While all* *cytokines were markedly stimulated by IL-1 alpha), co-addition of the* *cyclooxygenase inhibitor indomethacin enhanced IL-8 and GMCSF levels, but* *caused a reduction in IL-6 expression. The addition of PGE2 to cultures* *stimulated with IL-1 alpha and indomethacin resulted increases in IL-6 mRNA* *and protein expression while causing a concomitant reduction in GMCSF* *protein and mRNA expression. PGE2 and illoprost (PGI2 analog) enhanced IL-8* *production in stimulated cells. CONCLUSION. While PGE2 alone has limited* *effects on synovial cell production of IL-8 and GMCSF, its effects are* *significant in context of IL-1 alpha stimulation; endogenous PGE2 may alter* *cytokines secreted by mesenchymally derived cells. PGE2 may be an important* *modulator of cytokine driven inflammation.*
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* 4/3,AB/22*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*10454226 96260966 PMID: 8711266*
* Effect of rh-*GMCSF* and rh-GCSF on oxygen free radical production by* *human neutrophils and blood monocyte-derived human macrophages.* * al-Shammary F J; al-Zamel F; el-Shewemi S; Soliman R* * Department of Clinical Laboratory Sciences, College of Applied Medical* *Sciences, King Saud University, Saudi Arabia.*
* Renal physiology and biochemistry (SWITZERLAND) Nov-Dec 1995, 18 (6)* * p278-87, ISSN 1011-6524 Journal Code: 8906670*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The in vitro effect of recombinant human granulocyte-macrophage colony* *stimulating factor (rh-GMCSF) and recombinant human granulocyte colony* *stimulating factor (rh-GCSF) on oxygen free radical (OFR) generation by* *human neutrophils and blood monocytes derived human macrophages stimulated* *with phorbol myristate acetate was investigated and compared. The* *production of OFR by neutrophils and macrophages was time dependent, and* *the maximum release of OFR by neutrophils and macrophages was measured 90* *and 180 min after stimulation with phorbol myristate acetate, respectively.* *The priming effects or rh-GMCSF and rh-GCSF on OFR production by human* *neutrophils and macrophages was dose dependent. The maximum generation of* *OFR by neutrophils occurred when primed with 1,000 U/ml of rh-GMCSF and* *reached 2.383 +/- 0.191 nmol/10(5) neutrophils/90 min as compared with* *1.072 +/- 0.113 nmol/10(5) neutrophils/90 min in the unprimed controls.* *This represents a 122.20% increase in OFR generation ($p < 0.001$). However,* *the percentage of maximum increase in OFR production was 57.84 when* *neutrophils were primed with a concentration of 5,000 U of rh-GCSF/ml. In* *72-hour-old human macrophages, much higher levels of OFR production as* *compared with neutrophils were measured following stimulation with phorbol* *myristate acetate. The maximum generation of OFR was measured in* *macrophages primed for

45 min with 500 U/ml of rh-GMCSF. These cells* *produced 8.960 +/- 2.075 nmol/5 x 10(4) macrophage/180 min as compared with* *4.563 +/- 1.773 nmol/5 x 10(4) unprimed macrophages/180 min ($p < 0.001$). In* *macrophages primed with rh-GCSF, however, the maximum OFR production was* *induced by a dose of 5,000 U/ml and reached 6.902 +/- 1.463 nmol/5 x 10(4)* *macrophages/180 min as compared with 4.563 +/- 1.773 nmol/5 x 10(4)* *macrophages/180 min in the unprimed controls ($p < 0.05$). In conclusion, the* *priming effect of rh-GMCSF on OFR generation by human macrophages and* *neutrophils was more potent than that of rh-GCSF, both in the extent of* *augmentation and in the dose required to produce maximum OFR generation.* **
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* 4/3,AB/23*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*10394999 96200424 PMID: 8611477*
* The effect of the *GM*-*CSF*/IL-3 fusion protein PIXY321 on bone* *marrow and circulating haemopoietic cells of previously untreated patients* *with cancer.*
* Gheilmini M; Pettengell R; Coutinho L H; Testa N; Crowther D* * CRC Department of Medical Oncology, Christie Hospital, Manchester.* * British journal of haematology (ENGLAND) Apr 1996, 93 (1) p6-12,* *ISSN 0007-1048 Journal Code: 0372544*
* Document type: Clinical Trial; Clinical Trial, Phase I; Clinical Trial,* *Phase II; Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* This is a phase I/II study of the GM-CSF/IL-3 fusion protein (PIXY321.* *Patients were treated with PIXY321 at a daily subcutaneous dose of 500, 750* *and 1000 micrograms/m2 for 14 d. Side-effects were mild and consisted* *mainly of injection-site reactions and constitutional symptoms. A biphasic* *modest increase of white blood count (2-5-fold) and platelets (1-1.5 fold)* *was seen, accompanied by an increased bone marrow cellularity and an* *increase in circulating progenitors. Colony-forming cells in the blood rose* *to a median of 184 granulocyte/macrophage-colony forming cells (GM-CFC)/ml,* *eight Mix-CFC/ml, 250 burst forming units-erythroid (BFU-E)/ml and 140* *CFU-mega-karyocytes/ml, corresponding to a 10-, 2.5, 8- and 30-fold* *increase respectively. When seeded for long-term culture on irradiated bone* *marrow stroma, the mobilized cells were not able to sustain haemopoiesis in* *vitro to the same degree as bone marrow. Taken together these results* *indicate that PIXY321 has a biological effect in humans more similar to* *that of IL-3 than to that of GM-CSF.*
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* 4/3,AB/24*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*10387359 96192670 PMID: 8617583*
* Phase I trial of diaziquone (AZQ) plus *GM*-*CSF*.* * Hartmann L C; Ames M M; Reid J M; Richardson R L*
* Mayo Clinic, Rochester, MN 55905, USA.*
* Investigational new drugs (UNITED STATES) 1995, 13 (2) p175-6,* *ISSN 0167-6997 Journal Code: 8309330*
* Contract/Grant No.: CA15083; CA; NCI; CM07304; CM; NCI; M00585; PHS* * Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Diaziquone (AZQ) is a lipid soluble alkylating agent which was designed* *for increased CNS penetration. Its principle toxicity is myelosuppression.* *We conducted a phase I trial using AZQ in combination with GM-CSF to* *determine if the maximal tolerate dose (MTD) of AZQ could be escalated.* *Using GM-CSF on a standard schedule, we were unable to escalate the* *previously determined MTD of diaziquone with the use of this colony* *stimulating factor.*
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* 4/3,AB/25*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*10367281 96172085 PMID: 8580803*
* *GM*-*CSF* instead of hematological support during high-dose* *chemotherapy for refractory malignant lymphoma.*
* Aviles A; Nambo M J; Talavera A; Rosas A; Garcia E L; Diaz-Maqueo J C* * Department of Hematology, Oncology Hospital, National Medical Center* *Mexico, D.F. Mexico.*
* Leukemia & lymphoma (SWITZERLAND) Apr 1995, 17 (3-4) p327-30, ISSN* *1042-8194 Journal Code: 9007422*
* Document type: Clinical Trial; Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Patients with refractory malignant lymphoma (RML) have a poor prognosis* *when treated with conventional chemotherapy. The use of high-dose* *chemotherapy has been limited by secondary myelosuppression. We report the* *use of intensive and short-duration chemotherapy in patients with RML who* *received granulocyte-macrophage colony-stimulating factor (GM-CSF) instead* *of hematological support and salvage with bone marrow transplantation or* *infusion of peripheral blood stem cells. Thirty-one patients with RML were* *treated with

cyclophosphamide: 7 g/m2, iv on day 1, followed by GM-CSF: 5* *micrograms/kg/day, subcutaneously until hematological recovery* *(granulocytes > 1.8 x 10(9)/L) started on day 2. Methotrexate, 5 g/m2, was* *also given when the granulocytes and platelets counts were normal, followed* *by leucovorin rescue. Epirubicin, 180 mg/m2, iv, was given on day 29 if the* *granulocyte count was normal, and GM-CSF was started on day 30. Complete* *response was obtained in 21 out of 31 patients (67%) and partial response* *in 4 more, thus an overall response was achieved in 80% of the treated* *patients. Time to treatment failure was 24+ months, and the overall* *survival was 28+ months. Hematological toxicity grade IV, according to the* *WHO criteria was observed in all cycles, however hematological recovery was* *already evident on day 13 +/- 2. Eleven patients developed infection* *related to the treatment, but no therapy related death was observed. GM-CSF* *was well tolerated with minimal toxicity. Is evident that GM-CSF can act as* *hematological support after high-dose chemotherapy in patients who cannot* *undergo bone marrow transplantation programs.(ABSTRACT TRUNCATED AT 250* *WORDS)*

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* 4/3,AB/26*

*DIALOG(R)File 155:MEDLINE(R)*

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*10347823 96150312 PMID: 8552986*

* Adhesion of Plasmodium falciparum-infected erythrocytes to human cells* *and secretion of cytokines (IL-1-beta, IL-1RA, IL-6, IL-8, IL-10, TGF beta,* *TNF alpha, G-CSF, *GM*-*CSF*.*

* Wahlgren M; Abrams J S; Fernandez V; Bejarano M T; Azuma M; Torii M;* *Aikawa M; Howard R J*

* Department of Molecular Biology, DNAX Research Institute of Cellular and* *Molecular Biology Inc., Palo Alto, CA, USA.*

* Scandinavian journal of immunology (ENGLAND) Dec 1995, 42 (6)* * p626-36, ISSN 0300-9475 Journal Code: 0323767*

* Document type: Journal Article*

* Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* The scientific interest in the physical interaction of Plasmodium* *falciparum-infected erythrocytes with host cells stems from the suggestion* *that excessive binding in the microvasculature leads to severe malaria. The* *authors studied, therefore, two parasites for their ability to adhere to* *normal human cells and to induce cytokine production, one parasite lacking* *a binding capacity (DD2) and one which adhered to CD36+ transfected CHO* *cells (MCAMP). The MCAMP parasites readily bound to platelets and* *erythrocytes and to monocytes, polymorphonuclear granulocytes and* *EBV-transformed B cells as seen by light and electron microscopy. Platelets* *were frequently attached in large numbers to the infected erythrocyte* *surface and groups of infected erythrocytes were sometimes held together by* *several platelets. Nine out of 17 cytokines tested were found to be* *secreted into the culture supernatants after 35 h of co-cultures containing* *monocytes or unfractionated peripheral blood mononuclear cells (PBMC) and* *parasites (IL-1RA, IL-6, IL-8, IL-10, TGF beta, TNF alpha, G-CSF,* *IL-1-beta, and GM-CSF). Three additional cytokines were also present in low* *levels (< 200 pg/ml, IL-2, IL-4, IFN gamma) in the culture supernatants* *after incubation of the cells for 4 days. TNF alpha, IL-RA, and IL-8 were* *secreted from polymorphonuclear granulocytes, LGLs and T cells. Platelets* *and, to a lesser degree, monocytes and T cells secreted large amounts of* *TGF beta (10-30 ng/ml). Cytokines may participate in the pathogenesis but* *also the suppression of immune responses seen during acute malarial* *infections.*

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* 4/3,AB/27*

*DIALOG(R)File 155:MEDLINE(R)*

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*10333773 96136079 PMID: 8547128*

* *Platelets* prime PMN via released PF4: mechanism of priming and* *synergy with *GM*-*CSF*.*

* Aziz K A; Cawley J C; Zuzel M*

* Department of Haematology, University of Liverpool.* * British journal of haematology (ENGLAND) Dec 1995, 91 (4) p846-53,* *ISSN 0007-1048 Journal Code: 0372544*

* Document type: Journal Article*

* Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* Platelet-PMN interactions have been extensively studied and a spectrum of* *possible effects has been demonstrated. However, the physiological* *relevance of many of the observed in vitro phenomena remains obscure. Here* *we report a novel, and potentially pathophysiologically important,* *mechanism by which platelets can enhance PMN reactivity. We first observed* *that addition of platelets to PMN suspensions enhanced the* *chemiluminescence response of PMN to FMLP. This enhancement occurred* *without augmentation of superoxide generation and did not involve mutual* *platelet-PMN adhesion. The soluble material responsible was biochemically* *and immunologically identified as PF4 derived from platelet alpha-granules.* *The alpha-granule release was shown to be selective and required minimal* *platelet stimulation. Since the PF4 effect did not influence NADPH oxidase* *activation, it differed markedly from

that of other priming agents such as* *GM-CSF. Further studies showed that the PF4 effect was attributable* *entirely to the surface translocation and secretion of primary granule* *myeloperoxidase. There was marked synergy between PF4 and GM-CSF and both* *were required for maximal potentiation of PMN reactivity. These results* *demonstrate that PF4 and GM-CSF employ different pathways in PMN priming.* *The ease with which platelets could release PF4 at sites of vessel-wall* *damage and inflammation suggests that platelet-PMN interaction via PF4 is* *likely to be of major pathophysiological importance.* **
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* 4/3,AB/28*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*10324386 96126648 PMID: 8547862*
* A phase I trial of interleukin 3 (IL-3) pre-bone marrow harvest with* *granulocyte-macrophage colony-stimulating factor (*GM*-*CSF* )* *post-stem cell infusion in patients with solid tumors receiving high-dose* *combination chemotherapy.*
* Sosman J A; Stiff P J; Bayer R A; Peliska J; Peace D J; Loutfi S; Stock W* *; Oldenburg D; Unverzagt K; Bender J; et al*
* Division of Hematology/Oncology, Loyola University Medical Center,* *Maywood, IL 60153, USA.*
* Bone marrow transplantation (ENGLAND) Nov 1995, 16 (5) p655-61,* *ISSN 0268-3369 Journal Code: 8702459*
* Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* In humans, interleukin 3 (IL-3) administration increases the cellularity* *and cycling of bone marrow progenitor cell populations. Initially, in* *primates and then in humans, IL-3 in sequence with GM-CSF has been shown to* *stimulate multilineage hematopoiesis. Based upon these effects, we designed* *a phase I trial of daily IL-3 administered subcutaneously for 10 days at* *dose levels of 2.5, 5.0, 10.0, 12.5, and 15.0 micrograms/kg followed within* *72 h by bone marrow harvest, high-dose chemotherapy, and following* *chemotherapy, a fixed dose (5.0 micrograms/kg/day) of GM-CSF and bone* *marrow rescue. The study was designed to assess the toxicity and biological* *effects of IL-3 administered alone prior to bone marrow harvest and to* *determine the safety and clinical effects of IL-3 stimulated bone marrow* *with GM-CSF following high-dose combination chemotherapy. A total of 19* *patients with chemotherapy-sensitive non-hematologic malignancies (13* *breast, five ovarian, and one testicular cancer) were enrolled. IL-3 up to* *15.0 micrograms/kg/day could be administered without dose-limiting* *toxicities. Flu-like symptoms and headaches were common and poorly* *tolerated at the highest IL-3 dose. Significant increases in neutrophil* *counts (P = 0.018) were observed following IL-3. Overall, IL-3* *administration was associated with a modest, but significant increase in* *CFU-GM within the bone marrow (P = 0.034). IL-3 administration had no* *consistent effect on CD34+ cell number within bone marrow. For the entire* *group, engraftment of neutrophils to greater than 0.5 x 10(9)/l occurred at* *a median of 21 days (range of 13-63 days) and platelet independence* *occurred at a median of 17 days (range 11-120 days). When IL-3 dose levels* *were analyzed separately, engraftment of neutrophils and platelets, blood* *product (platelets and packed RBCs) utilization, and discharge date were* *not superior in those treated with the higher dose (15.0 micrograms/kg) of* *IL-3. While higher doses of IL-3 were associated with more toxicity, they* *did not appear to enhance the stem cell pool or speed engraftment later.* *The effects of pre-bone marrow harvest IL-3 are modest and likely not as* *impressive as other approaches aimed at enhancing hematologic recovery* *following high-dose chemotherapy.*
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* 4/3,AB/29*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*09242122 20555334 PMID: 11091498*
* Peripheral blood stem cell mobilization with cyclophosphamide in* *combination with G-CSF, *GM*-*CSF*, or sequential *GM*-* **CSF* /G-CSF in non-Hodgkin's lymphoma patients: a randomized* *prospective study.*
* Gazitt Y; Callander N; Freytes C O; Shaughnessy P; Liu Q; Tsai T W;* *Devore P*
* University of Texas, Health Science Center, Audie L. Murphy Memorial VA* *Hospital, San Antonio 78284, USA. gazitt@uthscsa.edu* * Journal of hematotherapy & stem cell research (UNITED STATES) Oct 2000,* * 9 (5) p737-48, ISSN 1525-8165 Journal Code: 100892915* * Document type: Clinical Trial; Journal Article; Randomized Controlled* *Trial*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* We designed a randomized, prospective three-arm mobilization study to* *determine the kinetics of peripheral blood stem cell (PBSC) mobilization in* *60 non-Hodgkin's lymphoma (NHL) patients primed with cyclophosphamide (CTX)* *in combination with granulocyte colony-stimulating factor (G-CSF) (arm A),* *granulocyte-macrophage (GM)-CSF (arm B) or GM-CSF/G-CSF (arm C). We also* *compared mobilization and transplant-related toxicities, pre- and* *post-transplant support and the probability of

survival among the three* *arms. To date, 35 patients have been enrolled in the study; 13 patients* *have been enrolled in arm A, 10 patients in arm B, and 13 patients in arm* *C. Successful collection of the target of > or = 2 X 10(6) CD34+ cells/kg* *in one to four apheresis collections was 10/13, 6/10, and 7/12 in arms A,* *B, and C, respectively. The differences between arms were not statistically* *significant. The median time to achieve the target CD34+ cells in patients* *who successfully mobilized the target CD34+ cells was 3 days, 2 days, and 1* *day, in patients in arms A, B, and C, respectively. The time for neutrophil* *engraftment was 11, 10, and 10 days in arms A, B, and C, respectively. The* *time for platelet engraftment was 11 days for patients in all arms of the* *study. Most importantly, no significant differences were observed among the* *three arms in the duration of neutropenic fever, the extent of mucositis,* *diarrhea, and nausea/vomiting, or in the number of units of platelets or* *red cells transfused after transplantation. Risk factors associated with* *poor mobilization were > or = 3 regimens of chemotherapy prior to* *mobilization, older age, and disease histology (follicular versus diffuse).* *Therefore, we conclude that the type of growth factor used for mobilization* *did not play a major role in the outcome of mobilization and recommend* *mobilizing NHL patients before they receive multiple regimens of* *chemotherapy.*
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* 4/3,AB/30*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08857577 20142671 PMID: 10678181*
* Nf1 and *Gmcsf* interact in myeloid leukemogenesis.* *
Birnbaum R A; O'Marcaigh A; Wardak Z; Zhang Y Y; Dranoff G; Jacks T;* *Clapp D W; Shannon K M*
* Department of Pediatrics, University of California, San Francisco* *94143-0519, USA.*
* Molecular cell (UNITED STATES) Jan 2000, 5 (1) p189-95, ISSN* *1097-2765 Journal Code: 9802571*
* Contract/Grant No.: CA72614; CA; NCI; CA74886; CA; NCI* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The NF1 tumor suppressor gene encodes neurofibromin, a GTPase-activating* *protein (GAP) for p21ras (Ras). Children with NF1 are predisposed to* *juvenile myelomonocytic leukemia (JMML). Some heterozygous Nf1 mutant mice* *develop a similar myeloproliferative disorder (MPD), and adoptive transfer* *of Nf1-deficient fetal liver cells consistently induces this MPD. Human* *JMML and murine Nf1-deficient cells are hypersensitive to* *granulocyte-macrophage colony-stimulating factor (GM-CSF) in* *methylcellulose cultures. We generated hematopoietic cells deficient in* *both Nf1 and Gmcsf to test whether GM-CSF is required to drive excessive* *proliferation of Nf1-/- cells in vivo. Here we show that GM-CSF play a* *central role in establishing and maintaining the MPD and that recipients* *engrafted with Nf1-/- Gmcsf-/- hematopoietic cells are hypersensitive to* *exogenous GM-CSF.*
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* 4/3,AB/31*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08711146 95399751 PMID: 7670096*
* Results of a phase I/II trial of recombinant human granulocyte-macrophage* *colony-stimulating factor in very low birthweight neonates: significant* *induction of circulatory neutrophils, monocytes, *platelets*, and bone* *marrow neutrophils.*
* Cairo M S; Christensen R; Sender L S; Ellis R; Rosenthal J; van de Ven C;* *Worcester C; Agosti J M*
* Children's Hospital of Orange County, CA 92668, USA.* * Blood (UNITED STATES) Oct 1 1995, 86 (7) p2509-15, ISSN 0006-4971* *Journal Code: 7603509*
* Document type: Clinical Trial; Clinical Trial, Phase I; Clinical Trial,* *Phase II; Journal Article; Randomized Controlled Trial* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Neonates, especially those of very low birthweight (VLBW), have an* *increased risk of nosocomial infections secondary to deficiencies in* *development. We previously demonstrated that granulocyte-macrophage* *colony-stimulating factor (GM-CSF) production and mRNA expression from* *stimulated neonatal mononuclear cells are significantly less than that from* *adult cells. Recombinant murine GM-CSF administration to neonatal rats has* *resulted in neutrophilia, increased neutrophil production, and increased* *survival of pups during experimental Staphylococcus aureus sepsis. In the* *present study, we sought to determine the safety and biologic response of* *recombinant human (rhu) GM-CSF in VLBW neonates. Twenty VLBW neonates (500* *to 1,500 g), aged < 72 hours, were randomized to receive either placebo (n* *= 5) or rhuGM-CSF at 5.0 micrograms/kg once per day (n = 5), 5.0* *micrograms/kg twice per day (n = 5), or 10 micrograms/kg once per day (n =* *5) given via 2-hour intravenous infusion for 7 days. Complete blood counts,* *differential, and platelet counts were obtained, and tibial bone marrow* *aspirate was performed on day 8. Neutrophil C3bi receptor expression was* *measured at 0 and 24 hours. GM-CSF levels were measured by a sandwich* *enzyme-linked immunosorbent assay at 2, 4, 6, 12, and 24 hours after the* *first dose of rhuGM-CSF. At all doses,

rhuGM-CSF was well tolerated, and* *there was no evidence of grade III or IV toxicity. Within 48 hours of* *administration, there was a significant increase in the circulating* *absolute neutrophil count (ANC) at 5.0 micrograms/kg twice per day and 10.0* *micrograms/kg once per day, which continued for at least 24 hours after* *discontinuation of rhuGM-CSF. When the ANC was normalized for each* *patient's first ANC, there was a significant increase in the ANC on days 6* *and 7 at each dose level. By day 7, all tested doses of rhuGM-CSF resulted* *in an increase in the absolute monocyte count (AMC) compared with* *placebo-treated neonates. In those receiving rhuGM-CSF 5.0 micrograms/kg* *twice per day, there was additionally a significant increase in the day 7* *and 8 platelet count. Tibial bone marrow aspirates demonstrated a* *significant increase in the bone marrow neutrophil storage pool (BM NSP) at* *5.0 micrograms/kg twice per day and 10.0 micrograms/kg once per day.* *Neutrophil C3bi receptor expression was significantly increased 24 hours* *after the first dose of rhuGM-CSF at 5.0 micrograms/kg once per day. The* *elimination half-life (T1/2) of rhuGM-CSF was 1.4 +/- 0.8 to 3.9 +/- 2.8* *hours.(ABSTRACT TRUNCATED AT 400 WORDS)*

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* 4/3,AB/32*

*DIALOG(R)File 155:MEDLINE(R)*

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*08538811 95227109 PMID: 7536072*

* Comparison of G-CSF with *GM*-*CSF* for mobilizing peripheral* *blood progenitor cells and for enhancing marrow recovery after autologous* *bone marrow transplant.*

* Bolwell B J; Goormastic M; Yanssens T; Dannley R; Baucco P; Fishleder A* * Bone Marrow Transplant Program, Cleveland Clinic Foundation, OH 44195.* * Bone marrow transplantation (ENGLAND) Dec 1994, 14 (6) p913-8,* *ISSN 0268-3369 Journal Code: 8702459*

* Document type: Clinical Trial; Controlled Clinical Trial; Journal Article* * Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* Primed peripheral blood progenitor cells (PBPC) with hematopoietic growth* *factors enhance marrow engraftment after autologous bone marrow* *transplantation (BMT). G-CSF and GM-CSF stimulate the production of PBPC;* *both cytokines alone also stimulate neutrophil recovery after autologous* *BMT. Little data exist comparing these two cytokines. We prospectively* *studied G-CSF and GM-CSF in autologous BMT. Forty-four consecutive patients* *with either Hodgkin's disease or non-Hodgkin's lymphoma underwent* *autologous BMT using both PBPC and autologous marrow. The autologous BMT* *preparative regimen was CBV (VP-16 2400 mg/m2, CY 1800 mg/m2 i.v. four* *times daily for 4 days, BCNU 600 mg/m2). Sixteen patients received G-CSF 5* *micrograms/kg sc daily for 8 days for mobilization of PBPC and received* *G-CSF 16 micrograms/kg i.v. four times daily after autologous BMT.* *Twenty-eight patients received GM-CSF to mobilize PBPC (14 patients* *received 250 micrograms/m2 sc daily for 8 days; 14 patients received 125* *micrograms/m2 sc twice daily for 8 days) and GM-CSF (250 micrograms/m2 i.v.* *four times daily) after autologous BMT. Patients underwent three to five* *pheresis procedures to harvest at least 3 x 10(8) nucleated cells/kg.* *Patients receiving G-CSF had higher peripheral WBC counts than did those* *receiving GM-CSF. Total numbers of mononuclear cells, total CD34+ cells and* *total CD34+/33-negative cells were similar in the two treatment groups. The* *patients receiving G-CSF after autologous BMT experienced a more rapid* *engraftment of both neutrophils (9 days vs 13 days, p = 0.0001) and* *platelets (14 days vs 18 days, p = 0.027) than did patients receiving* *GM-CSF after transplant.(ABSTRACT TRUNCATED AT 250 WORDS)*

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* 4/3,AB/33*

*DIALOG(R)File 155:MEDLINE(R)*

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*08398466 95086445 PMID: 7994241*

* In vivo effects of *GM*-*CSF* and IL-3 on hematopoietic cell* *recovery in bone marrow and blood after autologous transplantation with* *mafosfamide-purged marrow in lymphoid malignancies.*

* Albin N; Douay L; Fouillard L; Laporte J P; Isnard F; Lesage S; Ozsahin H* *; Bardinet D; Najman A; Gorin N C*

* Department of Hematology, Hopital Saint-Antoine, Paris, France.* * Bone marrow transplantation (ENGLAND) Aug 1994, 14 (2) p253-9,* *ISSN 0268-3369 Journal Code: 8702459*

* Document type: Journal Article*

* Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* This retrospective study evaluates the impact of GM-CSF and interleukin 3* *(IL-3) on bone marrow (BM) and peripheral blood (PB) cell recovery* *following autologous bone marrow transplantation (ABMT) with* *mafosfamide-purged BM in patients with lymphoid malignancies compared with* *a control group receiving no colony-stimulating factor. GM-CSF was* *administered at 250 micrograms/m2/day (8 patients) as a continuous infusion* *from day of autologous BMT until the absolute neutrophil count (ANC)* *reached 0.5 x 10(9)/l for 7 days or until day 30, whichever was first. IL-3* *was administered daily starting on the first day of transplant at a dose of* *1 microgram/kg/day (6 patients)

and 5 micrograms/kg/day (6 patients) for 30* *days. CFU-GM and BFU-E were sequentially evaluated in BM and PB at days 7,* *14, 21, 28, and 56 post-graft. The neutrophil recovery (ANC > 0.5 x* *10(9)/l) was significantly faster in the GM-CSF group compared with IL-3 5* *micrograms, IL-3 1 microgram and control group (respectively, days 15, 21,* *22, 24) ($p < 0.05$ to $p < 0.01$). Similarly, leukocyte recovery was faster in* *the GM-CSF group compared with control and IL-3 1 microgram groups ($p <$* *0.01 and $p < 0.05$). No difference was noticed between the two IL-3 groups.* *Although no difference was observed in platelet recoveries (> 50 x* *10(9)/l), it appeared that the GM-CSF group required more units of* *platelets than either the IL-3 1 microgram or 5 micrograms groups ($p <$* *0.05).(ABSTRACT TRUNCATED AT 250 WORDS)*

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* 4/3,AB/34*

*DIALOG(R)File 155:MEDLINE(R)*

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*08350374 95038345 PMID: 7950902*

* Prevention of hematopoietic myeloid and megakaryocyte toxicity associated* *with zidovudine in vivo in mice with recombinant *GM*-*CSF*.* * Gallicchio V S; Hughes N K; Tse K F*

* Department of Internal Medicine, Lucille P. Markey Cancer Center,* *University of Kentucky Medical Center, Lexington 40536-0084.* * Growth regulation (SCOTLAND) Jun 1994, 4 (2) p41-7, ISSN 0956-523X* *Journal Code: 9106990*

* Contract/Grant No.: CA-46509; CA; NCI*

* Document type: Journal Article*

* Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* We studied the effect of granulocyte-macrophage colony-stimulating factor* *(GM-CSF) on the suppression of hematopoiesis associated with the use of the* *antiviral drug zidovudine (AZT) administered in vivo to normal mice, as* *determined by measuring peripheral blood indices, and assays of* *hematopoietic progenitors, i.e. erythroid (CFU-E/BFU-E), myeloid (CFU-GM),* *and megakaryocyte (CFU-Meg) from bone marrow and spleen. Previous studies* *from this laboratory have established that dose-escalation zidovudine* *induced a dose-dependent decrease in hematocrit, WBC, and platelets with* *altered populations of bone marrow and splenic erythroid, myeloid and* *megakaryocyte progenitors when administered to normal mice. Daily* *administration of GM-CSF (10 micrograms/kg/bw) was associated with altered* *peripheral blood indices and progenitor cells. Dose-escalation AZT, i.e.* *0.1, 1.0 and 2.5 mg/ml, was associated with a comparable reduction in all* *indices, i.e. hematocrit, WBC, and platelets during the 6-week examination* *period. GM-CSF reduced zidovudine-induced myeloid toxicity (concentration <* *2.5 mg/ml) which was associated with an increase in bone marrow and splenic* *CFU-GM. High concentration, i.e. 2.5 mg/ml still produced myelosuppression* *irreversible with GM-CSF. GM-CSF induced a reduction in circulating* *platelets following zidovudine treatment at weeks 2 and 4 with the 1.0* *mg/ml and 2.5 mg/ml treatment groups respectively, compared to a persistent* *decrease in platelets in the presence of zidovudine alone. GM-CSF BFU-E* *were elevated indicating the restriction in erythoid differentiation was* *still present. These studies demonstrate GM-CSF influences myeloid and* *megakaryocyte recovery, but not the erythoid suppression associated with* *the antiviral drug zidovudine.*

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* 4/3,AB/35*

*DIALOG(R)File 155:MEDLINE(R)*

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*08341334 95029305 PMID: 7942785*

* Effect of low-dose granulocyte-macrophage colony-stimulating factor (LD-* **GM*-*CSF*) on platelet transfusion-dependent thrombocytopenia.* * Vesole D H; Jagannath S; Glenn L D; Barlogie B*

* Department of Medicine, University of Arkansas for Medical Sciences,* *Little Rock 72205.*

* American journal of hematology (UNITED STATES) Nov 1994, 47 (3)* * p203-7, ISSN 0361-8609 Journal Code: 7610369*

* Contract/Grant No.: CA 55819; CA; NCI*

* Document type: Clinical Trial; Journal Article*

* Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* Granulocyte-macrophage colony-stimulating factor (GM-CSF) is a* *hematopoietic growth factor known to promote the proliferation and* *differentiation of precursors of granulocytes and monocytes. GM-CSF at* *standard doses (125-500 micrograms/m2) alleviates neutropenia secondary to* *cytotoxic chemotherapy, myelodysplastic syndromes, and aplastic anemia, but* *has minimal effect on anemia or thrombocytopenia. GM-CSF at doses < 30* *micrograms/m2 has been reported to improve platelet counts in some patients* *exhibiting cytopenia related to hematologic disorders such as aplastic* *anemia and myelodysplastic syndrome. Low-dose GM-CSF (10-20 micrograms/m2)* *was evaluated in 20 patients with transfusion-dependent thrombocytopenia* *persisting after myeloablative cytotoxic chemotherapy or with* *disease-related cytopenia. Seven patients (35%) responded as defined by a* *reduction in the platelet transfusion requirements by at least 75%.* *Low-dose GM-CSF did not significantly increase neutrophil counts or* *decrease

red blood cell transfusion requirements. These results indicate* *that low-dose GM-CSF has a thrombopoietic effect in about one-third of* *patients with platelet transfusion-dependent thrombocytopenia which has not* *been observed at higher doses.*
**
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* 4/3,AB/36*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08289672 94355911 PMID: 8075592*
* PIXY321 (*GM*-*CSF* /IL-3 fusion protein): biology and early* *clinical development.*
* Vadhan-Raj S*
* Department of Clinical Immunology and Biological Therapy, University of* *Texas M. D. Anderson Cancer Center, Houston 77030.*
* Stem cells (Dayton, Ohio) (UNITED STATES) May 1994, 12 (3) p253-61,* *ISSN 1066-5099 Journal Code: 9304532*
* Document type: Journal Article; Review; Review, Tutorial* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Granulocyte-macrophage colony-stimulating factor (GM-CSF) and* *interleukin-3 (IL-3) are functionally related hematopoietins with* *overlapping but distinct hematopoietic effects. GM-CSF supports more* *myeloid progenitor cells, whereas IL-3 promotes more erythroid,* *megakaryocytic and multipotential progenitor cells. Their complementary in* *vivo biological effects and cross competition for receptor binding prompted* *the development of PIXY321, a synthetic hybrid protein of GM-CSF and IL-3.* *PIXY321 binds to cell lines expressing specific receptors for either* *ligand, and it exhibits enhanced biological activity in human hematopoietic* *progenitor cell assays. In preclinical studies, PIXY321 has been shown to* *accelerate both neutrophil and platelet recovery in rhesus monkeys* *subjected to sublethal irradiation. Based on these preclinical* *observations, clinical trials have been initiated examining the therapeutic* *potential of this agent in ameliorating treatment- or disease-related* *hematopoietic suppression. The early results indicate that PIXY321 can* *stimulate multilineage hematopoiesis in vivo and enhance neutrophil and* *platelet recovery following chemotherapy and bone marrow transplantation* *(BMT). These results suggest that PIXY321 elicits the biological effects of* *both its component cytokines and represents a novel means of delivering two* *independent but interactive cytokines in combination.* **
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* 4/3,AB/37*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08172310 94238231 PMID: 7514201*
* The role of G-CSF in mature neutrophil function is not related to* **GM*-*CSF*-type cell priming.*
* Treweeke A T; Aziz K A; Zuzel M*
* University Department of Haematology, Royal Liverpool University* *Hospital, England.*
* Journal of leukocyte biology (UNITED STATES) May 1994, 55 (5) p612-6* *, ISSN 0741-5400 Journal Code: 8405628*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Because of uncertainties regarding the comparability of* *granulocyte-macrophage and granulocyte colony-stimulating factors with* *regard to their effects on mature neutrophils (PMNs), we compared the* *actions of the two cytokines on reactive oxidant production and granular* *secretion by these cells. We found that chemiluminescence (CL) stimulated* *by formylmethionyl-leucyl-phenylalanine (fMLP) was not influenced by G-CSF* *(0.1-100 ng/ml), whereas GM-CSF priming (10 ng/ml) caused a nearly twofold* *increase in this PMN response. Moreover, the reactivity of PMNs treated* *with GM-CSF and G-CSF in combination was not different from that of PMNs* *treated with GM-CSF alone. GM-CSF (10 ng/ml) increased the rate of O2-* *production by 79%, caused a fivefold increase in fMLP-induced* *myeloperoxidase (MPO) secretion, and strongly enhanced CD11b expression. In* *contrast, G-CSF (50 ng/ml) only slightly increased O2- production (by 15%),* *and MPO secretion and CD11b expression remained unchanged. Both cytokines* *together gave results similar to those obtained with GM-CSF alone. In the* *presence of platelets (which by themselves enhanced PMN reactivity), the* *differences in the effects of the two cytokines persisted. We conclude that* *the priming effect of G-CSF on mature PMNs is negligible compared with that* *of GM-CSF. Our results are in conflict with previous reports of much more* *pronounced G-CSF effects but in accord with recent work showing the failure* *of this cytokine to induce a range of effects produced by GM-CSF. We* *therefore suggest that the primary role of G-CSF in mature PMN function is* *still unclear but may be related to the control of PMN distribution in view* *of the mobilizing and marginating effects of the cytokine in vivo.* **
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* 4/3,AB/38*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08161505 94227380 PMID: 8173195*
* [Phase I trial of recombinant human granulocyte-macrophage colony* *stimulating factor.

Results in patients with advanced tumors]* * Essai de phase I d'un granulocyte-macrophage colony-stimulating factor (* **GM*-*CSF*) humain recombinant. Resultats chez des malades atteints* *de tumeurs solides.*
* Berthaud P; Eugene-Jolchine I; Spielmann M; Le Chevalier T; Tursz T* * Service de medecine B, Institut Gustave-Roussy, Villejuif, France.* * Bulletin du cancer (FRANCE) May 1993, 80 (5) p418-30, ISSN* *0007-4551 Journal Code: 0072416*
* Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article;* *Randomized Controlled Trial ; English Abstract*
* Languages: FRENCH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Fourteen patients with advanced solid tumors were included in a phase I* *trial of recombinant human E coli derived granulocyte-macrophage*
*colony-stimulating factor (GM-CSF) given daily subcutaneously for 10* *consecutive days. Dose levels were increased from 250 micrograms/m2 to 500,* *750 and 1,000 micrograms/m2. Adverse effects were mainly fever, local* *irritation, lethargia, arthalgia. Three patients did not complete the* *10-day cycle: one patient died due to progressive disease without toxic* *effects related to GM-CSF, one was withdrawn because of suspicion of* *pulmonary embolism (not confirmed), one patient had hypotension, not* *recurring after treatment with GM-CSF. Although the maximum tolerated dose* *was not reached, the trial was stopped at 1,000 micrograms/m2, considering* *the satisfactory response and the high white blood cell counts observed* *with lower dose levels. N-fold increases of leucocyte count ranged between* *4.2 and 8.2 for the first dose level (250 micrograms/m2), 4 and 10.1 for* *500 micrograms/m2, 8.5 and 12.3 for 750 micrograms/m2 and 5.6 and 8.3 for* *1,000 micrograms/m2. Increases of granulocyte, neutrophil and eosinophil* *counts had a similar pattern with a weaker response at 1,000 micrograms/m2* *(two patients who completed the cycle). In contrast, even for the first* *three levels, no dose response relationship was shown for increases of* *monocytes (between 2.8 and 12 n-fold whatever the dose), or lymphocytes* *(between 1.7 and 10.7 n-fold whatever the dose). Decreases of platelets* *(between 6 and 55%) were observed, followed by a rebound after stopping* *treatment. No modifications of erythrocyte count were observed.* *Subcutaneous GM-CSF was well-tolerated up to 1,000 micrograms/m2 during a* *10-day course. Hematological effects were observed from the first dose* *level of 250 micrograms/m2.*
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* 4/3,AB/39*

*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08073095 94138844 PMID: 8306251*
* Cytokine intervention permits dose escalation of radioantibody. An* *analysis of myelostimulation by bolus versus continuous infusion of IL-1/* **GM*-*CSF*.*
* Blumenthal R D; Sharkey R M; Forman D; Wong G; Goldenberg D M* * Garden State Cancer Center, Center for Molecular Medicine and Immunology,* *Newark, New Jersey 07103.*
* Cancer (UNITED STATES) Feb 1 1994, 73 (3 Suppl) p1083-92, ISSN* *0008-543X Journal Code: 0374236*
* Contract/Grant No.: CA39841; CA; NCI; CA49995; CA; NCI* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* BACKGROUND. The authors recently reported that a 12-day schedule* *(beginning 3 days before radioantibody treatment) of twice-daily dosing of* *rH-IL-1 (1 x 10(3) U/dose) and rM-GM-CSF (0.5 micrograms/dose) can reduce* *the magnitude and duration of radioantibody-induced myelosuppression,* *thereby permitting a 25-30% increase in the dose of radioantibody that can* *be administered without the dose proving lethal. In an effort to further* *reduce toxicity and escalate the tolerated dose, the authors altered the* *method of administration of cytokines from daily bolus dosing to continuous* *infusion by implantable osmotic pumps. METHODS. A control group of mice was* *compared to five groups of mice that either did or did not receive a 340* *microCi dose of radioantibody, and received no cytokines, cytokines by* *bolus dosing, or cytokines by continuous infusion. For 4 weeks, peripheral* *white blood cell and thrombocyte counts and thymus and spleen weights were* *taken, marrow cell number was monitored, and marrow colony-forming unit* *activity was evaluated weekly in the untreated control mice and the treated* *mice. RESULTS. These studies demonstrated that after a dose of* *radioantibody, continuous dosing of cytokines resulted in higher white* *blood cell (WBC) and platelet values than if bolus delivery was used (day* *7, WBC: 110% vs. 59%; day 14, WBC: 85% vs. 62%; day 21, WBC: 98% vs. 42%;* *day 7, platelets: 122% vs. 51%; day 14, platelets: 159% vs. 72%; day 21,* *platelets: 239% vs. 171%). A comparison of bolus versus continuous dosing* *in the absence of radioantibody indicated that spleen weight increased by* *40-60% after continuous infusion of cytokines and by 20-25% after bolus* *dosing. The 20-30% decrease in thymus weight was similar with both dosing* *regimens. Colony-forming units (CFUs) in marrow increased from 30-35 in* *untreated mice to 50-55 in mice given cytokines by bolus injection, and to* *150-180 in mice given continuous infusion of

cytokines. Spleen CFUs* *exhibited an insignificant increase after bolus dosing of cytokines but* *increased almost fourfold after continuous dosing. Peak stimulation of* *marrow and spleen CFUs occurred 28 days after initiation of cytokine* *administration (2 weeks after cytokines administration was stopped). The* *probability of survival for 6 weeks after further dose escalation to 360* *microCi I-131-MN-14 immunoglobulin G was 16.4% +/- 8.6% after bolus dosing* *and 58.1% +/- 11.3% after continuous infusion of cytokines. CONCLUSIONS.* *Although continuous infusion of cytokines proved to be a better method of* *reducing hematopoietic toxicity, further dose escalation of* *radioimmunotherapy using the "pump" method of cytokine delivery was not* *possible. Cytokine intervention by either mode of delivery permits a 25*% *dose intensification without the dose becoming lethal. Further escalation* *is not feasible, possibly because of other end organ toxicity.* **
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* 4/3,AB/40*
*DIALOG(R)File 155:MEDLINE(R)*
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*08034254 94099983 PMID: 8274295*
* Prevention of the hematopoietic toxicity associated with zidovudine in* *vivo with IL-1 alone or in combination with *GM*-*CSF* administered* *to normal mice.*
* Gallicchio V S; Hughes N K; Tse K F; Gaines H*
* Department of Internal Medicine, Lucille P. Markey Cancer Center,* *University of Kentucky Medical Center, Lexington 40536-0084.* * Growth factors (Chur, Switzerland) (SWITZERLAND) 1993, 9 (3) p177-83* *, ISSN 0897-7194 Journal Code: 9000468*
* Contract/Grant No.: CA-46509; CA; NCI*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* We studied the effect of interleukin-1 (IL-1 alpha) either alone or* *administered with GM-CSF on the induction of hematopoietic toxicity* *associated with zidovudine (AZT) in vivo, as determined by peripheral blood* *indices, and assays of hematopoietic progenitors, i.e., erythroid (BFU-E),* *myeloid (CFU-GM), and megakaryocyte (CFU-Meg) cultured from bone marrow and* *spleen. Previous results reported from this laboratory have established* *dose-escalation of zidovudine to normal mice induced a dose-dependent* *decrease in hematocrit, WBC, and platelets with altered populations of* *marrow and splenic erythroid, myeloid and megakaryocyte progenitors. Daily* *administration of IL-1 alpha (recombinant murine, 5 u/animal) with or* *without GM-CSF (recombinant murine (10 micrograms/kg/bw) was associated* *with reduced AZT-toxicity as measured by increases in peripheral blood* *indices and progenitor stem cells, i.e., CFU-GM, CFU-Meg and BFU-E cultured* *from either bone marrow and spleen. The presence of GM-CSF amplified the* *effect observed with IL-1 especially with respect to myelopoiesis. These* *results demonstrate IL-1 with or without GM-CSF reverses AZT-hematopoietic* *toxicity when used in vivo.*
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**
* 4/3,AB/41*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07925229 93386061 PMID: 8374510*
* A *GM*-*CSF*/IL-3 fusion protein promotes neutrophil and platelet* *recovery in sublethally irradiated rhesus monkeys.*
* Williams D E; Dunn J T; Park L S; Frieden E A; Seiler F R; Farese A M;* *Macvittie T J*
* Department of Experimental Hematology, Immunex Corporation, Seattle,* *Washington 98101.*
* Biotechnology therapeutics (UNITED STATES) 1993, 4 (1-2) p17-29,* *ISSN 0898-2848 Journal Code: 8918082*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The effects of a human GM-CSF/IL-3 fusion protein (PIXY321) were examined* *in a primate model of rebound hematopoiesis following sublethal* *irradiation. The results demonstrated an enhanced rate of both neutrophil* *and platelet regeneration, as well as functional activation of circulating* *neutrophils.*
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* 4/3,AB/42*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07816308 93271847 PMID: 1845132*
* Clinical use of recombinant human hematopoietic growth factors (*GM*-* **CSF*, IL-3, EPO) in patients with myelodysplastic syndrome.* * Herrmann F; Mertelsmann R; Lindemann A; Ottmann O G; Seipelt G; Oster W;* *Hoelzer D; Ganser A*
* Department of Hematology and Oncology, University of Freiburg, Germany.* * Biotechnology therapeutics (UNITED STATES) 1991, 2 (3-4) p299-311,* *ISSN 0898-2848 Journal Code: 8918082*
* Document type: Clinical Trial; Clinical Trial, Phase I; Clinical Trial,* *Phase II; Controlled Clinical Trial; Journal Article* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* We have conducted several phase I/II clinical studies in a total of 65* *MDS patients utilizing recombinant human hematopoietic growth factors* *including GM-CSF, IL-3, and EPO. Twenty-seven

patients with MDS were* *treated with either continuous i.v. infusion or single daily s.c. injection* *of rhGM-CSF at dosages from 15 micrograms/m2 to 1000 micrograms/m2. All of* *them exhibited white cell responses during the treatment cycles, but no* *sustained rise in reticulocytes or platelets was recorded. In four of the* *patients, all with > or = 15% blast cells in the bone marrow, the* *percentage of circulating blast cells increased during treatment with* *rhGM-CSF (at dosages of 500 micrograms/m2 and 1000 micrograms/m2,* *respectively), although no leukemic conversion occurred. Of 9 patients* *treated so far with rhIL-3 at single daily s.c. dosages of 60* *micrograms/m2, all exhibited white cell responses; 8 exhibited significant* *improved platelet and reticulocyte counts. Nineteen further patients* *received rhEPO for a period of 14 weeks by s.c. (10,000 U five times* *weekly) or i.v. bolus administration (150-450 U/kg). None of these patients* *experienced an increase in white cell and platelet counts. A significant* *increase of the reticulocyte count was recorded in 3 patients only. Another* *strategy involves the recruitment of leukemic cells into the cell cycle by* *hematopoietic growth factors followed by treatment with cycle-specific* *cytostatic agents. Therefore in 10 patients administration of rhGM-CSF (250* *g/m2/day x 14, s.c.) was combined with Ara-C treatment (20 mg/m2/day x 14;* *s.c.). Initial results of this pilot study available in 5 patients* *indicated that this approach may control leukemic cell proliferation and* *may increase number of mature myeloid cells in both bone marrow and* *peripheral blood. A similar approach utilizing rhIL-3 in conjunction with* *Ara-C is on-going.*
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* 4/3,AB/43*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07775800 93231296 PMID: 8472812*
* Improved survival and marrow engraftment of mice transplanted with bone* *marrow of *GM*-*CSF*-treated donors.*
* Ballin A; Sagi O; Schiby G; Meytes D*
* Department of Haematology, Sackler School of Medicine, Tel Aviv, Israel.* * European journal of haematology (DENMARK) Mar 1993, 50 (3) p168-71,* *ISSN 0902-4441 Journal Code: 8703985*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Recombinant granulocyte-macrophage colony-stimulating factor (GM-CSF)* *administered to bone marrow (BM) transplant recipients is associated with* *earlier recovery. We have investigated the possibility of stimulating* *normal donor mice in vivo with GM-CSF. Donor balb/c mice were injected i.p.* *with GM-CSF (5000 u) or saline. Seventy-two hours later 5 x 10(5)BM cells* *from either GM-CSF-treated or control donors were infused into lethally* *irradiated (850 R) recipients. In the recipients of BM from GM-CSF-treated* *donors, significantly higher CFU-S and significantly higher survival rate* *(57% [n = 65]; vs. 30% [n = 63]; p < 0.05) were noted. Donor mice of the* *GM-CSF group did not differ in bone-marrow cellularity and composition from* *their controls. However, recipients of BM from GM-CSF-treated mice had* *higher blood counts of haemoglobin, leukocytes and platelets compared to* *controls. These data demonstrate that pretreatment of BM donors with GM-CSF* *may be of benefit in improving survival and marrow engraftment in mice.* **
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* 4/3,AB/44*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07699563 93154813 PMID: 1493941*
* Granulocyte-macrophage colony-stimulating factor (*GM*-*CSF*):* *what role in bone marrow transplantation?*
* Schuster M W*
* Div. of Oncology, North Shore University Hospital-Cornell University* *Medical College, NY 11030.*
* Infection (GERMANY) 1992, 20 Suppl 2 pS95-9, ISSN 0300-8126* *Journal Code: 0365307*
* Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article;* *Randomized Controlled Trial; Review; Review, Tutorial* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Infection during the period of bone marrow aplasia remains one of the* *major risks associated with high-dose chemotherapy and transplantation.* *Over the past several years, a number of investigators in Europe and North* *America have evaluated the use of GM-CSF in the setting of autologous bone* *marrow transplantation. These studies have almost all shown a hastening of* *myeloid engraftment. This, for the most part, has led to fewer serious* *infections and a decreased hospital stay for the GM-CSF treated patients.* *An overall survival advantage has not been noted. There has also not been* *any consistent multi-lineage effect. Future trials with combinations of* *sequentially used cytokines may lead to more rapid recovery of red blood* *cells and platelets in addition to granulocytes.*
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* 4/3,AB/45*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **

*07464508 92328052 PMID: 1626572*
* Very low doses of *GM*-*CSF* administered alone or with* *erythropoietin in aplastic anemia.*
* Kurzrock R; Talpaz M; Gutterman J U*
* Department of Clinical Immunology and Biological Therapy, University of* *Texas M.D. Anderson Cancer Center, Houston 77030.*
* American journal of medicine (UNITED STATES) Jul 1992, 93 (1) p41-8,* *ISSN 0002-9343 Journal Code: 0267200*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* PURPOSE AND RATIONALE: There has been no previously published experience* *with granulocyte-macrophage colony-stimulating factor (GM-CSF) at doses* *less than 15 micrograms/m2/d in patients with aplastic anemia, and most* *observations have been made at doses of 100 to 500 micrograms/m2/d (2.5 to* *12.5 micrograms/kg/d). The benefits of using considerably lower doses, if* *effective, should include a decrease in cost and in side effects. We have* *therefore used very low doses of GM-CSF to treat a group of patients with* *aplastic anemia. Additionally, since severe anemia is often a problem in* *these patients, we recently started administering erythropoietin along with* *the GM-CSF. Herein we report the results of very-low-dose GM-CSF therapy in* *patients with aplastic anemia and our preliminary findings in those* *individuals who received combination therapy. PATIENTS AND METHODS: We* *administered recombinant human GM-CSF subcutaneously at doses of 5 to 20* *micrograms/m2/d ("very-low-dose GM-CSF") to 12 patients with aplastic* *anemia. In addition, a 13th patient received erythropoietin together with* *the GM-CSF regimen, and three of the 12 individuals who initially received* *1 or more months of GM-CSF alone were later also given erythropoietin* *(4,000 U/d subcutaneously). RESULTS: In five of 12 patients (42%) treated* *with very-low-dose GM-CSF, an increase in neutrophil counts (2.0- to* *6.7-fold) was noted, and one of these subjects attained a bilineage* *response (neutrophil counts, 0.3 to 1.75 x 10(9)/L; platelet counts, 8 to* *169 x 10(9)/L). Moreover, a sixth patient showed a rise in platelet counts* *(19 to 80 x 10(9)/L) without a concomitant increase in neutrophils.* *Constitutional side effects were minimal. Combining erythropoietin and* *very-low-dose GM-CSF produced a bilineage response (neutrophils, 1.0 to 3.0* *x 10(9)/L; hemoglobin, 7.4 to 9.4 g/dL) in the one patient who received* *erythropoietin together with the GM-CSF from the time that GM-CSF was* *initiated. In one of the other patients who were given combination therapy,* *the addition of erythropoietin appeared to enhance the response; this* *patient demonstrated a neutrophil response to GM-CSF alone and a trilineage* *response (neutrophils, 0.8 to 3.75 x 10(9)/L; hemoglobin, 7.0 to 13.1 g/dL;* *and platelets, 10 to 34 x 10(9)/L) to the combination. No toxicity was* *associated with the addition of erythropoietin. CONCLUSIONS: Our* *observations suggest that (1) very low doses of GM-CSF (5 to 20* *micrograms/m2/d subcutaneously) may be used initially in neutropenic* *patients with aplastic anemia, and the dose subsequently increased only in* *patients who do not respond; and (2) the administration of erythropoietin* *together with GM-CSF is well tolerated, can augment responsiveness in some* *patients, and deserves further study.*
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* 4/3,AB/46*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07164137 92026344 PMID: 1928304*
* Cytokine influence on simian immunodeficiency virus replication within* *primary macrophages. TNF-alpha, but not *GMCSF* , enhances viral* *replication on a per-cell basis.*
* Walsh D G; Horvath C J; Hansen-Moosa A; MacKey J J; Sehgal P K; Daniel M* *D; Desrosiers R C; Ringler D J*
* Harvard Medical School, Department of Pathology, New England Regional* *Primate Research Center, Southborough, Massachusetts 01772-9102.* * American journal of pathology (UNITED STATES) Oct 1991, 139 (4)* * p877-87, ISSN 0002-9440 Journal Code: 0370502*
* Contract/Grant No.: AI25644; AI; NIAID; AI29855; AI; NIAID; RR00168; RR;* *NCRR*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The control of HIV-1 or SIV replication within macrophages is probably* *influenced by a variety of viral and cellular factors. Of the cellular* *factors, the authors have studied cytokine influence on SIV replication in* *vitro utilizing simian alveolar macrophages and uncloned SIVmacMTV, a* *macrophage-tropic variant. The approach allowed quantification of viral* *replication on a per-cell basis. As reported for HIV-1 replication in* *macrophages, TNF-alpha significantly increased SIV production in these* *macrophage cultures. GMCSF also resulted in marked increases in SIV gag* *protein in culture supernatants. However, after correcting for differences* *in total cell numbers and numbers of gag-containing cells in the treated* *and untreated cultures, GMCSF did not upregulate SIV production on a* *per-cell basis. IL-6 increased SIV replication little if at all but induced* *significantly greater cytopathic changes in the treated

cultures compared* *with infected, untreated cultures. In contrast, IFN-gamma greatly decreased* *replication. Our results for GMCSF, IFN-gamma, and IL-6 are in contrast to* *previously published reports of cytokine control of HIV-1 growth in target* *cells, and they stress the importance of cell number analyses and the use* *of primary cultures in the study of lentiviral replication kinetics in* *macrophages.*
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* 4/3,AB/47*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07139280 92001460 PMID: 1911339*
* Megakaryocyte potentiating activity of IL-1, IL-6 and *GM*-*CSF** * as evaluated by their action on in vitro human megakaryocytic colonies.* * Takahashi T; Tsuyuoka R; Ueda Y; Suzuki A; Ichiba S; Okuno Y; Nakamura K;* *Imura H*
* Second Department of Internal Medicine, Kyoto University School of* *Medicine, Japan.*
* British journal of haematology (ENGLAND) Aug 1991, 78 (4) p480-7,* *ISSN 0007-1048 Journal Code: 0372544*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* We examined whether recombinant cytokines enhance the in vitro platelet* *production of interleukin-3 (IL-3)-induced human megakaryocytic colonies* *(Meg-colony). We classified Meg-colonies into four categories based on* *platelet production during in situ observation on day 14: type 0, absence* *of cytoplasmic processes in a colony; type 1, one to three processes in at* *least one megakaryocyte in a colony; type 2, four to eight processes; type* *3, more than nine processes or division of cytoplasm. Type 3 colonies were* *considered to be platelet-producing. In control cultures, type 1* *Meg-colonies were dominant, followed by type 2, type 3 and type 0. Of the* *cytokines added at the initiation of culture, interleukin-1 alpha (IL-1* *alpha), interleukin-6 (IL-6), and granulocyte/macrophage colony stimulating* *factor (GM-CSF) significantly increased the number of colonies.* *Furthermore, these three cytokines significantly elevated the proportion of* *type 3 colonies. Interleukin-4 (IL-4), granulocyte-CSF, macrophage-CSF and* *erythropoietin did not affect the colony count or distribution of colony* *type. IL-1 alpha, IL-6 and GM-CSF also significantly elevated the* *proportion of type 3 colonies, even when added to the culture on days 8 or* *11. These results indicate that IL-1 alpha, IL-6 and GM-CSF promote* *platelet production of in vitro Meg-colonies.*
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* 4/3,AB/48*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07105982 91347027 PMID: 1878735*
* Human recombinant *GM*-*CSF* in allogeneic bone marrow* *transplantation for leukaemia: double-blind placebo controlled trial.* * Powles R; Treleaven J; Millar J; Gordon-Smith E C; Tiley C; Findlay M;* *Teo C; Duncombe A; Robinson G*
* Royal Marsden Hospital, Sutton.*
* Bone marrow transplantation (ENGLAND) 1991, 7 Suppl 2 p85-6, ISSN* *0268-3369 Journal Code: 8702459*
* Document type: Clinical Trial; Journal Article; Randomized Controlled* *Trial*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* A double-blind randomised trial compared 20 patients with leukaemia* *receiving human recombinant granulocyte macrophage colony stimulating* *factor (GM CSF), with 20 patients receiving placebo for 14 days after* *allogeneic matched sibling bone marrow transplantation. The median* *neutrophil count at 14 days was significantly higher in the GM CSF group* *(1.90 vs. 0.46 x 10(9)/l). The duration of hospital stay, the number of* *antibiotic days, and the number of fever days was the same for both patient* *groups. The lymphocyte count was significantly higher in the GM-CSF group* *than in the placebo group between days 10 and 15 after transplantation. The* *GM-CSF group had lower haemoglobin concentrations and platelets counts, and* *higher plasma urea creatinine and bilirubin, than the placebo group. There* *was no evidence that GM CSF was associated with a greater incidence of* *leukaemic relapse.*
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* 4/3,AB/49*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06971227 91211719 PMID: 2020313*
* The hematopoietic growth factor *GM*-*CSF* in chemotherapy for* *advanced breast carcinoma]*
* Hematopoetische groeifactor *GM*-*CSF* bij chemotherapie wegens* *voortgeschreden mammacarcinoom.*
* Hoekman K; Wagstaff J; Boven E; van Groeningen C J; Vermorken J B; Pinedo* *H M*
* Academisch Ziekenhuis, Vrije Universiteit, afd. Geneeskundige Oncologie,* *Amsterdam.*
* Nederlands tijdschrift voor geneeskunde (NETHERLANDS) Mar 9 1991, 135* * (10) p415-9, ISSN 0028-2162 Journal Code: 0400770* * Document type: Clinical Trial; Journal Article ; English Abstract* * Languages: DUTCH*

* Main Citation Owner: NLM*
* Record type: Completed*
* A non-randomized study was carried out in the Free University Hospital,* *Amsterdam, to investigate the (hematologic) toxicity and antitumor response* *of patients with advanced breast cancer treated with intensive chemotherapy* *in combination with granulocyte-macrophage colony-stimulating factor* *(GM-CSF). Of 11 patients with an inoperable or metastasized breast cancer,* *5 were treated with doxorubicin 75 mg/m2 + cyclophosphamide 750 mg/m2* *intravenously every 3 weeks and 6 patients with 90 and 1000 mg/m2* *respectively. When in a preceding cycle a significant hematologic toxicity* *was observed, this patient was treated in the subsequent cycle with the* *same dose of chemotherapy in combination with GM-CSF 250 micrograms/m2/day* *from day 2-12 as a continuous infusion. Bone marrow depression was* *diminished in the presence of GM-CSF. This was apparent from a milder* *decline of the number of neutrophilic granulocytes, reduction of the* *neutropenic period and a more rapid recovery of the neutrophil number. A* *transient eosinophilia and a mild monocytosis were also observed. GM-CSF* *did not improve erythrocyte and thrombocyte counts. The efficacy of GM-CSF* *was less pronounced in the group of patients with the highest dose of* *chemotherapy. GM-CSF was associated with malaise, fever and a small* *decrease of blood pressure, which in combination with a frequently* *occurring anemia and the side-effects of high dose chemotherapy, resulted* *in a substantial toxicity. In 9/11 patients an objective tumor regression* *was noted. GM-CSF stimulated the recovery of granulocytes after intensive* *chemotherapy. Treatment of a small group of patients with advanced breast* *cancer with intensive chemotherapy resulted in a high antitumor response.* **
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* 4/3,AB/50*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06950147 91190624 PMID: 2012752*
* Effects of low doses of recombinant human granulocyte-macrophage colony* *stimulating factor (*GM*-*CSF* ) in patients with myelodysplastic* *syndromes.*
* Estey E H; Kurzrock R; Talpaz M; McCredie K B; O'Brien S; Kantarjian H M;* *Keating M J; Deisseroth A B; Gutterman J U*
* Department of Hematology, University of Texas, M. D. Anderson Cancer* *Center, Houston 77030.*
* British journal of haematology (ENGLAND) Mar 1991, 77 (3) p291-5,* *ISSN 0007-1048 Journal Code: 0372544*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* There has been no previously published experience with* *granulocyte-macrophage colony stimulating factor (GM-CSF) doses less than* *12 micrograms/m2 daily in patients with myelodysplastic syndromes, and most* *observations have been made at doses greater than or equal to 120* *micrograms/m2 daily. We administered 5 micrograms/m2 daily by subcutaneous* *injection to 29 such patients increasing the dose in patients who did not* *show a haematologic response. Doses of 5 or 10 micrograms/m2 ('low-dose* *GM-CSF') produced an increase in neutrophils in 14/29 patients. Response* *was significantly (P = 0.03) more frequent in patients who had a higher* *pre-treatment neutrophil count (e.g. 11/16 in patients with greater than or* *equal to 0.5 x 10(9)/l). A rise in blasts followed administration of* *low-dose GM-CSF in five patients, all with either refractory anaemia with* *excess blasts (RAEB) or refractory anaemia with excess blasts in* *transformation (RAEBT). Platelets decreased in five patients, four of whom* *had no change in blasts, reverting to baseline when GM-CSF was* *discontinued. We and others have previously observed similar rises in* *blasts or decreases in platelets at doses of 120 micrograms/m2 daily.* *Low-dose GM-CSF produced no constitutional side effects. Our results* *suggest that low doses of GM-CSF might be initially employed in neutropenic* *patients with myelodysplastic syndromes who present with pretreatment* *neutrophil counts greater than 0.5 x 10(9)/l. Increasing the dose, and* *hence the risk of extramedullary toxicity, only in patients who do not* *respond to the low dose. Patients who present with lower pre-treatment* *neutrophil counts might begin treatment at doses above 10 micrograms/m2,* *but below the 120 micrograms/m2 commonly employed, which may be necessary* *in relatively few patients.*
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* 4/3,AB/51*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06754232 90380462 PMID: 1976016*
* Large-scale collection of circulating haematopoietic progenitors in* *cancer patients treated with high-dose cyclophosphamide and recombinant* *human *GM*-*CSF*.*
* Ravagnani F; Siena S; Bregni M; Sciorelli G; Gianni A M; Pellegris G* * Istituto Nazionale Tumori, Milan, Italy.*
* European journal of cancer (Oxford, England - 1990) (ENGLAND) 1990, 26* * (5) p562-4, ISSN 0959-8049 Journal Code: 9005373* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*

* Record type: Completed*
* Circulating haematopoietic progenitors from 36 cancer patients were* *collected by continuous-flow leukapheresis during the phase of rapid* *haematopoietic recovery after pancytopenia induced by high-dose* *cyclophosphamide and then cryopreserved for autologous transplantation. 20* *of the patients also received intravenous infusion of recombinant human* *granulocyte macrophage-colony stimulating factor (rhGM-CSF) for 7, 10 or 14* *days after cyclophosphamide. 106 leukapheresis procedures were done for 2-5* *consecutive days. Leukapheresis was started significantly earlier in* *patients receiving rhGM-CSF. In these patients, yields of peripheral blood* *elements (leucocytes, mononuclear cells, haematopoietic progenitors and* *platelets) were significantly higher than in controls treated with* *cyclophosphamide only. In particular, the mean number of* *granulocyte-monocyte colony-forming cells was 43.88 X 10(4) vs. 6.16 X* *10(4) per kg patient body weight per leukapheresis. Side-effects of* *leukapheresis were limited to central venous catheter occlusion and fever* *in 4% and 2% of all procedures, respectively.*
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* 4/3,AB/52*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06734095 90360132 PMID: 2202477*
* Pretreatment with rh-*GMCSF*, but not rh-IL3, enhances PAF-induced* *eosinophil accumulation in guinea-pig airways.*
* Sanjar S; Smith D; Kings M A; Morley J*
* Preclincal Research, Sandoz Ltd., Basel, Switzerland.* *
British journal of pharmacology (ENGLAND) Jul 1990, 100 (3) p399-400* *, ISSN 0007-1188 Journal Code: 7502536*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Intraperitoneal injections of recombinant human granulocyte-macrophage* *colony stimulating factor (rh-GMCSF, 50 micrograms/kg-1 daily) or* *interleukin-3 (rh-IL3, 50 micrograms kg-1 daily) for two days, induced an* *increase in the percentage of bone marrow and pulmonary airway eosinophils* *in the guinea-pig. In addition, rh-IL3-treated animals exhibited an* *increase (21%) in blood neutrophils. Exposure of guinea-pigs to an aerosol* *of platelet activating factor (PAF) gives rise to a selective pulmonary* *eosinophil accumulation, maximal at 48 h. The eosinophilic response to PAF* *was significantly enhanced in rh-GMCSF-treated guinea-pigs but was* *suppressed in rh-IL3-treated animals.*
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* 4/3,AB/53*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06592325 90217668 PMID: 2182741*
* Human *GM*-*CSF* in vivo: identification of the target cells and* *of their kinetics of response.*
* Aglietta M; Bussolino F; Piacibello W; Apra F; Sanavio F; Stacchini A;* *Monzeglio C; Carnino F; Gavosto F*
* Clinica Medica A, Dipartimento di Scienze Biomediche ed Oncologia Umana,* *Italy.*
* International journal of cell cloning (UNITED STATES) Jan 1990, 8* *Suppl 1 p283-90; discussion 290-2, ISSN 0737-1454 Journal Code: 8308172* *
Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Granulocyte-macrophage colony-stimulating factor (GM-CSF) was given for* *three days (8 micrograms/kg/day) to 14 subjects who had solid tumors and* *normal hemopoiesis. The treatment induced a rapid 3- to 5-fold increase in* *the number of circulating neutrophils, eosinophils and monocytes.* *Lymphocytes, platelets and reticulocytes were unmodified during treatment.* *Activation of circulating neutrophils during GM-CSF treatment was* *demonstrated by a significant, increased release of neutrophil-derived* *platelet-activating factor after stimulation with N-formyl-methionyl-leucyl* *-phenylalanine, tumor necrosis factor-alpha or phagocytosis. The* *granulomonocytosis was dependent on increased bone marrow production of* *mature cells. Using the thymidine suicide technique, we observed that* *GM-CSF more than doubled the percentage of granulocyte-macrophage and* *megakaryocyte colony-forming units (CFU-gm and CFU-meg) and erythroid* *burst-forming units (BFU-e) in the S phase of the cell cycle. However, at* *the level of morphologically recognizable cells with autoradiography, we* *observed that GM-CSF increased the labeling index of the* *granulo-monopoietic cells, whereas that of the erythroblasts was unchanged.* *These data suggest that in accordance with in vitro observations, GM-CSF* *exerts its activity through all granulo-monopoietic lineages, whereas other* *cytokines (erythropoietin, thrombopoiesis-stimulating factors) may be* *needed to fully exploit the proliferative stimulus of GM-CSF on BFU-e and* *CFU-meg. After treatment discontinuation, the proliferative activity drops* *to values lower than before treatment, suggesting a period of relative* *refractoriness of marrow progenitors to the cytocidal effect of cell* *cycle-specific antineoplastic agents. This hypothesis is under evaluation* *in a controlled clinical trial where

GM-CSF is given prior to chemotherapy.* **
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* 4/3,AB/54*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06585932 90211244 PMID: 2182018*
* Changes in the expression of elastase and cathepsin B with* *differentiation of U937 promonocytes by *GMCSF*.* * Ward C J; Crocker J; Chan S J; Stockley R A; Burnett D* * General Hospital, Birmingham, England, U.K.*
* Biochemical and biophysical research communications (UNITED STATES) Mar* *16 1990, 167 (2) p659-64, ISSN 0006-291X Journal Code: 0372516* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The human promonocytic cell line, U937, when treated for up to 72h with*
*12,O,tetradecanoyl-phorbol-13-acetate or granulocyte-macrophage colony-stim* *ulating factor, exhibited increased phagocytic activity and expression of* *the marker p150/95. There was an associated increase in the monocyte* *proteinase cathepsin B and its mRNA but decreased cellular levels of* *neutrophil elastase and elastase mRNA. Granulocyte-macrophage* *colony-stimulating factor therefore causes differentiation of U937 cells,* *with appropriate effects on the synthesis of leukocyte proteinases.* **
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* 4/3,AB/55*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06556662 90181882 PMID: 2697435*
* Failure to immortalise human AML cells using human recombinant* **GMCSF* in vitro and in vivo.*
* Clutterbuck R; Newman A; Powles R; Kwong Y; Millar J; Shepherd V; Smith C* * Leukaemia Unit, Royal Marsden Hospital, Sutton, U.K.* * Bone marrow transplantation (ENGLAND) Dec 1989, 4 Suppl 4 p40-1,* *ISSN 0268-3369 Journal Code: 8702459*
* Document type: Clinical Trial; Journal Article; Randomized Controlled* *Trial*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* We have failed to find any evidence that human recombinant GM-CSF can* *immortalize human AML cells grown in liquid culture or as nodules in immune* *deprived mice. In previous clinical studies and a controlled trial* *currently underway there is no evidence of irreversible acceleration of the* *disease.*
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* 4/3,AB/56*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06515646 90140658 PMID: 2694367*
* Combined *GM*-*CSF* and erythropoietin therapy in myelodysplastic* *syndrome]*
* Kombinierte *GM*-*CSF* - und Erythropoietintherapie bei* *myelodysplastischem Syndrom.*
* Egli F; Hofer S; Greminger P; Rhyner K*
* Departement fur Innere Medizin, Universitatsspital Zurich.* * Schweizerische medizinische Wochenschrift (SWITZERLAND) Dec 9 1989,* *119 (49) p1777-80, ISSN 0036-7672 Journal Code: 0404401* * Document type: Journal Article ; English Abstract*
* Languages: GERMAN*
* Main Citation Owner: NLM*
* Record type: Completed*
* A 60-year-old patient with a myelodysplastic syndrome (MDS) corresponding* *to refractory anemia with an increase in blast cells (RAEB) was treated* *with granulocyte-macrophage colony stimulating factor (GM-CSF) and* *erythropoietin (EPO) for severe symptomatic pancytopenia. During the GM-CSF* *treatment a distinct increase in granulocytes was observed, but the* *reticulocytes and thrombocytes decreased to the point where treatment had* *to be discontinued after eight days. After subsequent treatment with EPO* *the reticulocyte count rose from 0% to 2%. However, this rise alone was* *insufficient to decrease the number of blood transfusions required. The* *thrombocyte count rose to the original values after the cessation of GM-CSF* *therapy while continuing treatment with EPO. Bone marrow investigations* *were performed before and after GM-CSF treatment and indicated a distinct* *increase in the myeloid precursor cells after therapy, without an increase* *in blasts. On the other hand, an obvious decrease in erythro- and* *megakaryopoiesis was observed.*
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* 4/3,AB/57*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06445672 90070368 PMID: 3077728*
* 5' region of zeta-globin and *GMCSF* genes share binding site for* *nuclear proteins.*
* Howard O M; Kane C; Deisseroth A*
* Department of Hematology, University of Texas M.D. Anderson Cancer* *Center, Houston 77030.*
* Transactions of the Association of American Physicians (UNITED STATES)* *1988, 101 p180-4, ISSN 0066-9458 Journal Code: 7506109* * Contract/Grant No.: RO1 29300; PHS*
* Document type: Journal Article*

* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
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* 4/3,AB/58*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06378872 90003259 PMID: 2529042*
* Murine T helper cell clones secrete granulocyte-macrophage* *colony-stimulating factor (*GmCSF*) by both interleukin-2-dependent and* *interleukin-2-independent pathways.*
* Wong R L; Lingenheld E G; Fitzgerald L; Clark R B*
* Department of Medicine, University of Connecticut Health Center,* *Farmington 06032.*
* Cellular immunology (UNITED STATES) Oct 15 1989, 123 (2) p445-55,* *ISSN 0008-8749 Journal Code: 1246405*
* Contract/Grant No.: AM-20621; AM; NIADDK*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Granulocyte-macrophage colony-stimulating factor (GmCSF) is a lymphokine* *secreted by class II major histocompatibility complex (MHC)-restricted T* *cells after lectin or antigen stimulation. To investigate the relationship* *between interleukin-2 (IL-2) and GmCSF production, we utilized long-term* *cultures of porcine myelin basic protein (PMBP)-specific T helper cell* *clones that were maintained with IL-2 in the absence of antigen or* *irradiated antigen-presenting cells (APC). We have found that supernatants* *of these T cell clones contained GmCSF activity after IL-2 stimulation.* *Inhibition of cell proliferation by irradiation failed to stop GmCSF* *production. When these clones were stimulated with PMBP and irradiated APC* *in the presence of anti-IL-2 receptor antibody, the T cell supernatants* *still contained GmCSF activity. These results indicate that (1) GmCSF* *production by T helper clones after IL-2 stimulation is independent of cell* *proliferation and (2) antigen/MHC-stimulated GmCSF production by T cell* *clones can occur by an IL-2-independent pathway.*
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* 4/3,AB/59*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06213641 89229375 PMID: 2653458*
* Human interleukin-5 (IL-5) regulates the production of eosinophils in* *human bone marrow cultures: comparison and interaction with IL-1, IL-3,* *IL-6, and *GMCSF*.*
* Clutterbuck E J; Hirst E M; Sanderson C J*
* National Institute for Medical Research, London, UK.*
* Blood (UNITED STATES) May 1 1989, 73 (6) p1504-12, ISSN 0006-4971* *Journal Code: 7603509*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Recombinant human interleukin-5 (rhIL-5), in either liquid or semi-solid* *cultures, selectively induced eosinophil production from normal human bone* *marrow, with no activity on other cell lineages. The time course of* *eosinophil production induced by murine IL-5, rhIL-3, and rh* *granulocyte-macrophage colony stimulating factor (GMCSF) was similar to* *rhIL-5. The rate of eosinophil maturation in vitro was independent of the* *stimulating cytokine, mature eosinophils being produced after 4 to 5 weeks* *in liquid culture with each of these cytokines. The eosinophils produced in* *response to each cytokine were morphologically indistinguishable, and had* *the ultrastructural features of maturity except that the electron-dense* *material in the granules had not formed into crystalline cores. Neither* *rhIL-1 nor rhIL-6 alone, or in combination with rhIL-5 or rhIL-3, induced* *eosinophil differentiation or proliferation under the conditions used.* *rhIL-3 and rhGMCSF induced more eosinophil colonies than rhIL-5, rhIL-5 had* *an additive, not synergistic, effect on eosinophil colony production when* *combined with either rhIL-3 or rhGMCSF, suggesting that rhIL-5 stimulates a* *smaller and possibly different population of eosinophil progenitors.* *However, rhIL-5 induced the greatest eosinophil production in liquid* *cultures, suggesting that although it may act on a smaller population of* *precursors, it is able to stimulate more proliferative steps than either* *rhIL-3 or rhGMCSF.*
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* 4/3,AB/60*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05840616 88194548 PMID: 2834073*
* A novel human macrophage-activating factor: distinction from* *interferon-gamma (IFN-gamma) and granulocyte-macrophage colony-stimulating* *factor (*GMCSF*).*
* Jones M P; Gunapala D E; Matutes E; Catovsky D; Coates A R* * Department of Medical Microbiology, London Hospital Medical College,* *England.*
* Cellular immunology (UNITED STATES) May 1988, 113 (2) p361-75,* *ISSN 0008-8749 Journal Code: 1246405*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*

* Culture supernatant from a human T-cell leukemia virus type I* *(HTLV-1)-infected cell line, DGA-1, contained a novel macrophage-activating* *factor (MAF). This MAF was antigenically and functionally distinct from* *interferon-gamma (IFN-gamma) and from granulocyte-monocyte* *colony-stimulating factor (GMCSF). Potential contaminants such as bacterial* *lipopolysaccharide (LPS), Mycoplasma spp, and HTLV-1 were not responsible* *for this MAF activity. The DGA-1 MAF was secreted constitutively and the* *cell line grew well in the absence of growth factors such as interleukin-2,* *mitogen, or antigen. This cell line should provide a good source of this* *MAF for further purification and characterization.*
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* 4/3,AB/61*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05672476 88025609 PMID: 3311210*
* The effect of recombinant *GM*-*CSF* on the recovery of monkeys* *transplanted with autologous bone marrow.*
* Monroy R L; Skelly R R; MacVittie T J; Davis T A; Sauber J J; Clark S C;* *Donahue R E*
* Immunobiology and Transplantation Department, Naval Medical Research* *Institute, Bethesda, MD 20814-5055.*
* Blood (UNITED STATES) Nov 1987, 70 (5) p1696-9, ISSN 0006-4971* *Journal Code: 7603509*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The regulatory function of recombinant human granulocyte-macrophage* *colony stimulating factor (rhGM-CSF) on granulocyte production in vivo was* *evaluated in an autologous bone marrow transplantation model using rhesus* *monkeys. Monkeys were exposed to 9.0 Gy total body irradiation and then* *transplanted with 5.0 x 10(7) low-density bone marrow cells/kg. Alzet* *miniosmotic pumps were subcutaneously implanted to deliver rhGM-CSF at a* *rate of 50,400 U/kg/d. Minipumps, containing either rhGM-CSF or saline,* *were implanted between zero and five days after transplantation for seven* *days. Kinetic recoveries of peripheral blood cells after either saline or* *rhGM-CSF treatment were compared. Treatment with rhGM-CSF accelerated the* *recovery of neutrophils. Neutrophils in rhGM-CSF-treated animals recovered* *to 80% (3.4 x 10(3)/mm3) pre-irradiation control levels by day 20, in* *comparison with only 33% (0.9 x 10(3)/mm3) recovery for saline control* *monkeys. In addition, the recovery of neutrophils was enhanced over that of* *the controls, reaching 140% v 70% on day 30. Another prominent feature of* *rhGM-CSF-treated monkeys was the accelerated recovery of platelets,* *reaching near 50% normal levels by day 24 in comparison with 20% of normal* *levels for controls. The infusion of rhGM-CSF was shown to be an effective* *regulator of early hematopoietic regeneration, leading to the accelerated* *recovery of both neutrophils and platelets and then providing a consistent* *sustained increase of neutrophils even in the absence of rhGM-CSF.* **
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* 4/3,AB/62*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05601354 87280726 PMID: 3301903*
* Recombinant human granulocyte-macrophage colony-stimulating factor (* **GM*-*CSF* ) shortens the period of neutropenia after autologous* *bone marrow transplantation in a primate model.*
* Nienhuis A W; Donahue R E; Karlsson S; Clark S C; Agricola B; Antinoff N;* *Pierce J E; Turner P; Anderson W F; Nathan D G*
* Journal of clinical investigation (UNITED STATES) Aug 1987, 80 (2)* * p573-7, ISSN 0021-9738 Journal Code: 7802877*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The effect of granulocyte-macrophage colony-stimulating factor (GM-CSF)* *on hematopoietic reconstitution after autologous bone marrow* *transplantation was evaluated in a primate model. Animals were given a* *continuous intravenous infusion of recombinant human GM-CSF for several* *days both before and after transplantation or only after the transplant* *procedure. Marrow ablation was accomplished by total body irradiation. In* *both groups of animals, the neutrophil count reached 1,000/mm3 by 8-9 d* *posttransplant compared with an interval of 17 and 24 d for two concurrent* *controls. After withdrawal of GM-CSF, neutrophil counts fell to values* *comparable to those observed in untreated controls. Accelerated recovery of* *platelet production was also observed in four of the five animals. Two* *additional animals were initially given GM-CSF several weeks* *posttransplantation because of inadequate engraftment. Prompt and sustained* *increases in neutrophil and platelet counts were observed. We conclude that* *GM-CSF may be useful in accelerating bone marrow reconstitution.* **
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* 4/3,AB/63*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05563714 87242927 PMID: 3496133*
* Recombinant human *GM*-*CSF* induces leukocytosis and activates* *peripheral blood polymorphonuclear

neutrophils in nonhuman primates.* * Mayer P; Lam C; Obenaus H; Liehl E; Besemer J*
* Blood (UNITED STATES) Jul 1987, 70 (1) p206-13, ISSN 0006-4971* *Journal Code: 7603509*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The in vivo efficacy of glycosylated and nonglycosylated recombinant* *human granulocyte macrophage colony-stimulating factor (rh GM-CSF)* *expressed in Chinese hamster ovary cells and Escherichia coli respectively* *was studied in rhesus monkeys following a daily subcutaneous (SC; three* *times) or intravenous (IV; over six hours) dose for seven consecutive days.* *The monkeys responded to the rh GM-CSF with a prompt (within 24 hours) rise* *in circulating white blood cells (WBCs). Thereafter the total cell counts* *increased steadily in a dose-dependent manner with repeated dosing to* *numbers six times over the pretreatment levels. Overall, granulocyte counts* *increased fivefold, lymphocytes twofold to fourfold, and monocytes* *threefold to fourfold. Platelets and erythrocytes were unaffected. Within 1* *week after the end of treatment the leukocytosis had disappeared. Of the* *two routes of treatment, SC (three times daily)-administered rh GM-CSF was* *more effective than the same dose given by a six-hour IV infusion. In* *addition to inducing leukocytosis, parenterally administered rh GM-CSF* *primed mature circulating granulocytes for enhanced oxidative metabolism* *and killing of an E coli strain. These results show that exogenously* *administered glycosylated or nonglycosylated rh GM-CSF is both an effective* *stimulator of leukocytosis and a potent activator of the phagocytic* *function of mature granulocytes in monkeys.*
*? ds*
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*Set Items Description*
*S1 355 LEUKOCYTOSIS AND THROMBOCYTOPENIA*
*S2 28 S1/TI*
*S3 357 GMCSF OR GM()CSF AND PLATELETS*
*S4 63 S3/TI*
*? s leukocytopenia*
* S5 514 LEUKOCYTOPENIA*
*? s s5 and thrombocytopenia*
* 514 S5*
* 24787 THROMBOCYTOPENIA*
* S6 192 S5 AND THROMBOCYTOPENIA*
*? s s6 and thrombopoietin*
* 192 S6*
* 1859 THROMBOPOIETIN*
* S7 0 S6 AND THROMBOPOIETIN*
*? s s6 and (gmcsf or gm()csf)*
* 192 S6*
* 155 GMCSF*
* 25852 GM*
* 43880 CSF*
* 9861 GM(W)CSF*
* S8 2 S6 AND (GMCSF OR GM()CSF)*
*? t s8/3,ab/all*
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* 8/3,AB/1*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*11251480 98129051 PMID: 9467870*
* Uteroferrin and recombinant bovine *GM*-*CSF* modulate the* *myelosuppressive effects of 5-fluorouracil in young female pigs (Sus* *scrofa).*
* Laurenz J C; Hadjisavas M; Schuster D; Bazer F W*
* Department of Animal Science, Texas A&M University, College Station* *77843-2471, USA.*
* Comparative biochemistry and physiology. Part B, Biochemistry & molecular* *biology (ENGLAND) Nov 1997, 118 (3) p569-77, ISSN 1096-4959* *Journal Code: 9516061*
* Contract/Grant No.: DK 46766; DK; NIDDK*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The present study investigated the ability of uteroferrin and recombinant* *bovine granulocyte monocyte/macrophage-colony stimulating factor (rbGM-CSF)* *to modulate the myelosuppressive effects of 5-fluorouracil (5-FU) in young* *female pigs (Sus scrofa). Pigs (N = 3/treatment) were infused with 5-FU* *(32.5 mg/kg) on days 0 and 1 of the experimental period. Uteroferrin (100* *micrograms/kg in 0.9% NaCl), rbGM-CSF (10 micrograms/kg in 0.9% NaCl),* *uteroferrin + rbGM-CSF (as above) or control (0.9% NaCl) were administered* *as intramuscular injections twice daily (0800 and 2000 hr). Peripheral* *blood cell number, composition, and progenitor cells were determined over* *28 days. Treatment of pigs with 5-FU resulted in a rapid* **leukocytopenia* and *thrombocytopenia* (nadirs on days 5 and 7,* *respectively) and a modest decrease ($P < 0.05$) in red blood cell (RBC)* *number (nadir on day 14). Although nor affecting RBC and thrombocytes,* *treatment of pigs with uteroferrin had an initial protective effect (P <* *0.05) on the 5-FU-induced *leukocytopenia* (63 and 64 vs 48 and 39 +/-* *6% of baseline on days 3 and 5, respectively). In contrast, rbGM-CSF* *enhanced ($P < 0.05$) the rate of the *leukocytopenia* and had only minor* *effects on thrombocyte numbers relative to controls. These effects appeared* *to be additive, as pigs treated with uteroferrin + rbGM-CSF had a reduced* *rate of *leukocytopenia* compared to pigs treated with rbGM-CSF alone.* *Uteroferrin + rbGM-CSF also

attenuated (P < 0.05) the suppression and* *enhanced (P < 0.05) recovery of RBC and thrombocyte numbers following 5-FU* *treatment. In control pigs, a modest rebound leukocytosis (122 +/- 6% of* *baseline) and thrombocytosis (141 +/- 9% of baseline) was evident.* *Uteroferrin enhanced (P < 0.05) the rebound leukocytosis (135 +/- 6% of* *baseline), but attenuated (P < 0.05) the thrombocytosis. In contrast,* *rbGM-CSF enhanced (P < 0.05) the duration of the leukocytosis during the* *recovery phase, an effect augmented by the combination of uteroferrin +* *rbGM-CSF. In addition, treatment with uteroferrin + rbGM-CSF resulted in a* *sustained thrombocytosis (days 12 to 21). As indicated by changes in* *CFU-GM, BFU-E, and CFU-GEMM progenitor cells in peripheral blood, the* *effects of uteroferrin and rbGM-CSF appeared to reflect their ability to* *enhance the proliferation and/or differentiation of both similar and* *distinct hematopoietic progenitor cells.*
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* 8/3,AB/2*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05896790 88251104 PMID: 2838001*
* [Therapy of the preleukemic state: effect of androgens on refractory* *anemia]*
* Sakurada K; Morioka M; Miyazaki T*
* 3rd Dept. of Internal Medicine, Hokkaido University School of Medicine.* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jun 1988, 15 (6)* * p1960-7, ISSN 0385-0684 Journal Code: 7810034*
* Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* We have examined the efficacy of various drugs in 44 patients with MDS* *and found the different effectiveness which depends on the type of MDS.* *Namely, RA appears to respond to steroid hormone, androgen, and/or vitamin* *D3, regardless of single or combined use. In particular, it is obvious in* *androgen, and as our previous reports, high content of acidic ferritin in* *RBC with RA have changed to more basic ones by treatment with androgen. On* *the contrary, these drugs were not effective on RAEB, RAEB-T, and CMML. A* *long-term observation is needed to determine whether the prolonged or* *decreased occurrence of leukemia could be obtained in the effective cases* *with RA. Most of the cases who did not develop overt leukemia during this* *study died of bleeding or infections due to *thrombocytopenia* or* **leukocytopenia* , thus indicating that supportive therapies are* *important in patients with MDS. Since it has recently been reported that* *recombinant G-CSF or *GM*-*CSF* is helpful to increase the number* *of leucocyte and to enhance their functional recovery in MDS, these factors* *may be powerful agents against infections when they are carefully used with* *regard to the activation of leukemic clones.*
*? ********ds*
*? ds*
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*Set Items Description*
*S1 355 LEUKOCYTOSIS AND THROMBOCYTOPENIA*
*S2 28 S1/TI*
*S3 357 GMCSF OR GM()CSF AND PLATELETS*
*S4 63 S3/TI*
*S5 514 LEUKOCYTOPENIA*
*S6 192 S5 AND THROMBOCYTOPENIA*
*S7 0 S6 AND THROMBOPOIETIN*
*S8 2 S6 AND (GMCSF OR GM()CSF)*
*? s s6 and thrombopoietin*
* 192 S6*
* 1859 THROMBOPOIETIN*
* S9 0 S6 AND THROMBOPOIETIN*
*? s s6 not s8*
* 192 S6*
* 2 S8*
* S10 190 S6 NOT S8*
*? s s10 and py<1996*
* 190 S10*
* 8815308 PY<1996*
* S11 110 S10 AND PY<1996*
*? s s11 and py<1995*
* 110 S11*
* 8398613 PY<1995*
* S12 99 S11 AND PY<1995*
*? t s12/3,ab/all*
**
* 12/3,AB/1*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08463392 95151608 PMID: 7661927*
* Phase II study of carboplatin and etoposide as a first line regimen in* *patients with metastatic breast cancer.*
* van der Gaast A; Bontenbal M; Planting A S; Kok T C; Splinter T A* * Department of Medical Oncology, Rotterdam Cancer Institute, The* *Netherlands.*
* Annals of oncology - official journal of the European Society for Medical* *Oncology / ESMO (NETHERLANDS) Nov *1994*, 5 (9) p858-60, ISSN* *0923-7534 Journal Code: 9007735*
* Comment in Ann Oncol. 1995 Apr;6(4) 403; Comment in PMID 7619757* * Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* BACKGROUND: The data available on the role of carboplatin and etoposide* *in breast cancer, especially in patients with no or minimal prior therapy* *are limited.

PATIENTS AND METHODS: We performed a phase II study with* *carboplatin and etoposide as first line treatment in 34 patients with* *metastatic breast cancer. The treatment regimens was carboplatin 300 mg/m2* *day 1, and etoposide 100 mg/m2 days 1, 3 and 5 every four weeks. RESULTS:* *Of 33 evaluable patients, 2 achieved complete responses (6%) lasting 4 and* *5 months, 7 patients (21%) achieved partial responses with a median* *duration of 6+ (range 5-8) months, 15 patients had stable disease, and 9* *progressed during treatment. The major toxicity was myelosuppression WHO* *grades 3 or 4 *leukocytopenia* or *thrombocytopenia* were seen in* *15 and 10 patients, respectively. One formally ineligible patient with an* *impaired renal function died 14 days after the start of treatment because* *of a septicaemia in the presence of a grade 4 *leukocytopenia*. Besides* *this patient no other patient presented with granulocytopenic fever.* *CONCLUSION: In view of the observed response rate of 27% (95% confidence* *interval 11%-43%) we think that carboplatin and etoposide given in this* *dose and schedule has probably no clear advantage over the more commonly* *used regimens.*
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* 12/3,AB/2*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08389474 95077450 PMID: 7986118*
* [Chemotherapy of brain tumors]*
* Kuratsu J; Ushio Y*
* Dept. of Neurosurgery, Kumamoto University Medical School.* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Oct *1994*, 21* *Suppl 3 p377-83, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article; Review; Review, Tutorial ; English* *Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Despite recent attempts to improve chemotherapeutic approaches for the* *treatment of malignant gliomas, results remain limited and palliative. The* *development of effective chemotherapy for tumors of the central nervous* *system (CNS) is complicated in that the blood-brain barrier (B.B.B.)* *hampers the penetration of most drugs into the brain and cerebrospinal* *fluid. The factors governing delivery in the brain are the drug's molecular* *weight, lipophilicity and degree of ionization. Now the standard therapy* *for malignant glioma is maximal tumor resection followed by combination* *radiotherapy plus chemotherapy. Nitrosoureas are representative drugs which* *easily cross the B.B.B.. It has been shown that nitrosourea compounds have* *an additive effect to radiotherapy. The toxicity profile of nitrosoureas is* **leukocytopenia* and *thrombocytopenia* as a dose-limiting factor.* *Furthermore, the great heterogeneity of malignant glioma tissues offered a* *rationale for the use of multiple drugs. Many studies were reported to show* *a substantial advantage for the multidrug regimen over control series* *utilizing single drugs alone. Despite clear examples of the effectiveness* *of chemotherapy, we are still far from improving the cure rate for the vast* *majority of patients with primary malignancies of the CNS. Further* *improvement in patient survival may depend upon understanding and* *manipulating the pathways that regulate aberrant growth in these tumors.* *The development of new anticancer agents, which are sensitive to malignant* *glioma and can reach a high concentration in glioma tissue, is warranted.* **
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* 12/3,AB/3*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08330353 95018323 PMID: 7932808*
* Phase II study of gemcitabine (2',2'-difluorodeoxycytidine) in previously* *treated ovarian cancer patients.*
* Lund B; Hansen O P; Theilade K; Hansen M; Neijt J P* * Department of Oncology, Rigshospitalet, University Hospitals of* *Copenhagen, Denmark.*
* Journal of the National Cancer Institute (UNITED STATES) Oct 19* **1994*, 86 (20) p1530-3, ISSN 0027-8874 Journal Code: 7503089* * Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article;* *Multicenter Study*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* BACKGROUND: Platinum-containing combination chemotherapy has resulted in* *improved survival rates in patients with advanced ovarian carcinoma, but* *the majority of the patients still die of their disease. It is therefore* *important to develop new non-cross-resistant drugs. Gemcitabine* *(2',2'-difluorodeoxycytidine) has shown a broad spectrum of antineoplastic* *activity in tumor cell cultures in vitro and in animal tumor models.* *Clinical activity also has been reported in a variety of solid tumor types.* *PURPOSE: Our purpose was to assess the clinical activity of gemcitabine in* *previously treated ovarian cancer patients and to further characterize the* *toxicity of the compound. METHODS: Gemcitabine (800 mg/m2) was given* *intravenously once a week for 3 consecutive weeks, followed by 1 week of* *rest. A maximum of two different prior treatment regimens was allowed.* *Response was assessed by pelvic examination and/or ultrasound and computed* *tomography scans every other course. RESULTS: Fifty patients were eligible;* *35 (70%) had bulky disease

(tumor greater than 5 cm in diameter). All* *patients had received prior platinum-containing combination chemotherapy.* *Forty-two patients were assessable for response. Eight (19%) of the 42* *patients (95% confidence interval = 9%-34%) achieved a partial response,* *with a median response duration of 8.1 months (range, 4.4-12.5 months). All* *responders started treatment with gemcitabine within 6 months of prior* *treatment, and seven of the eight responders were resistant to first-line* *platinum-containing combination chemotherapy. Overall median time to* *progression was 2.8 months (range, 0.2 12.5 months), and overall median* *survival was 6.2 months (range, 0.2-26.0 months). Forty-eight patients were* *assessable for toxicity. *Leukocytopenia* and *thrombocytopenia** *were the main toxic effects that caused dose omissions (27% and 14%,* *respectively) and dose reductions (37% and 21%, respectively). A transient* *mild flu-like syndrome occurred in 28% of the patients, and* *treatment-related peripheral edema developed in 22%. Grade 1 hematuria (53*% *of patients), grade 1-2 proteinuria (79% of patients), and liver toxicity* *that was mostly grade 1-2 (59% of patients) were also observed.* *CONCLUSIONS: Gemcitabine is a well-tolerated new drug with activity in* *platinum-resistant ovarian cancer patients. IMPLICATIONS: Confirmatory* *trials are needed, and the activity of gemcitabine in previously untreated* *patients should be assessed.*
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* 12/3,AB/4*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08277644 94343710 PMID: 8065019*
* [Parvovirus B19-induced aplastic crisis in a patient with iron deficiency* *anemia]*
* Negami T; Ohta M; Okuda K; Shimizu S*
* Takaoka City Hospital, Department of Internal Mediacine, Toyama, Japan.* * Rinsho ketsueki The Japanese journal of clinical hematology (JAPAN) Jul* **1994*, 35 (7) p670-5, ISSN 0485-1439 Journal Code: 2984782R* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* A 38-year-old female was referred to Takaoka City Hospital for treatment* *of common-cold-like symptom and an episode of transient unconsciousness.* *Physical examination on admission revealed severe anemia and an ejection* *heart murmur. Complete blood count revealed microcytic hypochromic anemia* *(Hb 4.1 g/dl), *leukocytopenia* (2.600/microliters),* **thrombocytopenia* (7.1 x 10(4)/microliters) and reticulocytopenia* *(17,000/microliters). The bone marrow cellularity was within normal limits.* *Cells in the erythroid series were decreased to 5% of total bone marrow* *nucleated cells with maturation arrest at the level of proerythroblasts.* *Giant proerythroblasts were observed in 0.2% of marrow nucleated cells. No* *stainable iron was seen. Both anti-parvovirus B19 IgM antibody and IgG* *antibody were positive in the serum and parvovirus B19 DNA was detected in* *the bone marrow cells by polymerase chain reaction. From these results,* *iron deficiency anemia complicated with pure red cell aplasia secondary to* *parvovirus B19-induced infection was diagnosed. The anemia gradually* *improved with administration of sodium ferrous citrate one month after* *admission. Parvovirus B19 has been reported to cause an aplastic crisis in* *the patients who has a rapid red cell turn over such as hemolytic anemia or* *acute blood loss. This report suggested that severe aplastic crisis is also* *induced in patients with iron deficiency anemia by parvovirus B19-induced* *infection and warns that careful observation is necessary for the follow up* *of patients with iron deficiency anemia.*
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* 12/3,AB/5*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*08197743 94263665 PMID: 8204353*
* 5-Fluorouracil, folinic acid, etoposide and cisplatin chemotherapy for* *locally advanced or metastatic carcinoma of the oesophagus.* * Stahl M; Wilke H; Meyer H J; Preusser P; Berns T; Fink U; Achterrath W;* *Knipp H; Harstrick A; Berger M; et al*
* Department of Internal Medicine (Cancer Research), University of Essen,* *Germany.*
* European journal of cancer (Oxford, England - 1990) (ENGLAND)* **1994*, 30A (3) p325-8, ISSN 0959-8049 Journal Code: 9005373* * Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* 38 patients with advanced oesophageal carcinoma were treated with* *intravenous (i.v.) folinic acid (300 mg/m2), 5-fluorouracil (500 mg/m2),* *etoposide (100 mg/m2), and cisplatin (30 mg/m2) (FLEP), on days 1, 2 and 3,* *every 22-28 days. 26 patients had locally advanced disease (LAD) and 12 had* *metastatic disease (M1). Oesophagectomy was planned for patients with LAD* *in case of tumour regression after chemotherapy, while patients with M1* *disease received chemotherapy only. The overall remission rate was 45*% *(17/38) including four clinical and two pathologically confirmed complete* *remissions. 16 patients underwent oesophagectomy, 12 after response to* *FLEP, and 4 after FLEP and subsequent irradiation +/-*

*5-fluorouracil/mitomycin. Toxicity was mainly haematological, with WHO* *grade 3 and 4 *leukocytopenia* in 50% and *thrombocytopenia* in 31*% *of the patients. Two treatment-related deaths were observed; one due to* *chemotherapy and one postoperatively. Median survival time of LAD patients* *was 13 months, and actuarial 2-year survival was 31%. Patients with* *complete tumour resection after FLEP had a median survival time of 18* *months and a 2-year survival rate of 42%. Median survival of M1 patients* *was 6 months. FLEP is an active combination for oesophageal cancer,* *especially when used preoperatively in LAD.*
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* 12/3,AB/6*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07871195 93326880 PMID: 8392880*
* [Herbal decoction of qingwen baidu yin in treating endotoxic fever in* *rabbits]*
* Xie T*
* Hangzhou Hospital of TCM.*
* Zhongguo zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi =* *Chinese journal of integrated traditional and Western medicine / Zhongguo* *Zhong xi yi jie he xue hui, Zhongguo Zhong yi yan jiu (CHINA) Feb* **1993*, 13 (2) p94-7, 69, ISSN 1003-5370 Journal Code: 9211576* * Document type: Journal Article ; English Abstract*
* Languages: CHINESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Qingwen Baidu Yin (QBY) has good curative effects on the endotoxic fever* *of rabbits induced by injecting endotoxin of E. Coli. The test group was* *given QBY orally, while the control group was given NS orally instead.* *Result showed QBY could: (1) Markedly inhibit the fever, it was effective* *in reducing febrile curve. delta T and TRI5 of the test group were smaller* *(P < 0.001). (2) Ameliorate the *leukocytopenia* and leukocytosis, and* *improve *thrombocytopenia*. (3) Antagonize hyperviscosity syndrome and* *had the actions of depolymerization and dilution. (4) In test group, the* *increased cAMP content in plasma was reduced, and the decreased cGMP* *content raised, the ratio of cAMP and cGMP was nearly normal. All these* *provided the clue in elucidating the essence of "Excessive Yang causes* *Heat" and "Predominance of Yang leads to disorder of Yin". (5)* *Pathomorphological examination showed that QBY had the functions of* *protecting the internal organs and reducing the organic damage induced by* *endotoxing in rabbits.*
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* 12/3,AB/7*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07851795 93307467 PMID: 8319786*
* *Thrombocytopenia* induced by human parvovirus B19 infections.* * Yoto Y; Kudoh T; Suzuki N; Katoh S; Matsunaga Y; Chiba S* * Department of Pediatrics, School of Medicine, Sapporo Medical University,* *Japan.*
* European journal of haematology (DENMARK) May *1993*, 50 (5)* * p255-7, ISSN 0902-4441 Journal Code: 8703985*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Human parvovirus B19 (B19) has a remarkable tissue-tropism for erythroid* *elements--from erythroid precursors (BFU-E, CFU-E) to erythroblasts. B19 is* *thought to be incapable of propagating in cells other than erythroid* *progenitors. *Leukocytopenia* and *thrombocytopenia* sometimes* *occur in addition to erythrocytopenia in patients with B19 infection. We* *retrospectively investigated the possible cause of *thrombocytopenia** * by B19 infection in 23 patients with *thrombocytopenia* admitted to* *our hospital in the past 5 years. Two patients were found to be infected by* *B19. Mild *thrombocytopenia* in both cases was thought to be an early* *event in B19 infection.*
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* 12/3,AB/8*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*07805291 93260826 PMID: 8492412*
* [Cyclosporine therapy of adult onset Still's disease with disseminated* *intravascular coagulation]*
* Mori T; Tanigawa M; Iwasaki E; Tamaki S; Ono T; Wada H; Deguchi K;* *Shirakawa S*
* Second Department of Internal Medicine, Mie University School of* *Medicine.*
* Rinsho ketsueki The Japanese journal of clinical hematology (JAPAN) Feb* **1993*, 34 (2) p147-52, ISSN 0485-1439 Journal Code: 2984782R* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* In April, 1991, a 61-year-old man was admitted to our hospital because of* *pancytopenia and disseminated intravascular coagulation (DIC). Five years* *prior to admission he had developed high fever, skin eruption and* *arthralgia which had been improved by antibiotics, but recurred. Steroid* *therapy was ineffective for pancytopenia and DIC. Laboratory findings were* *as follows: RBC count, 274 x 10(4)/microliters;

WBC count, 470/microliters;* *Platelets, 6.4 x 10(4)/microliters; fibrinogen, 153mg/dl; FDP, 67.0* *micrograms/ml; FDP-D.Dimer, 13040ng/ml; thrombin-antithrombin complex, >* *60.0ng/ml; and plasmin alpha 2-plasmin inhibitor complex, 10.3* *micrograms/ml. As we suspected adult onset Still's disease on the basis of* *clinical course, we treated him with methylprednisolone pulse therapy,* *which was, however, ineffective. *leukocytopenia*, *thrombocytopenia% %% and DIC improved after cyclosporine treatment. Since cyclosporine is known to be very effective to autoimmune diseases, we speculate that in this patient immunological mechanism may be involve in the pathogenesis of DIC.

12/3,AB/9
DIALOG(R)File 155:MEDLINE(R)
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07659464 93114665 PMID: 1473755
Neoadjuvant intraarterial infusion chemotherapy with a combination of mitomycin-C, vincristine, and cisplatin for locally advanced cervical cancer: a preliminary report.
Itoh N; Sawairi M; Hanabayashi T; Mori H; Yamawaki Y; Tamaya T Department of Obstetrics and Gynecology, Gifu University School of Medicine, Japan.
Gynecologic oncology (UNITED STATES) Dec *1992*, 47 (3) p391-4, ISSN 0090-8258 Journal Code: 0365304
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Combination chemotherapy including cisplatin was administered intraarterially from the internal iliac artery as neoadjuvant chemotherapy to six patients with locally advanced uterine cervical cancer (stage higher than IIIB of FIGO). The drugs and doses were mitomycin-C 10 mg/m2, vincristine 1 mg/m2, and cisplatin 50 mg/m2. Two or three courses were repeated at intervals of 3 weeks. In three patients, dose reductions were undertaken for decreased renal function and *thrombocytopenia*. Partial response was, however, observed in all patients (response rate 100%), and five of six patients were able to undergo a radical hysterectomy. The major toxic effects were *leukocytopenia* , nausea, and vomiting. Our preliminary experience suggests that pelvic intraarterial infusion of combination chemotherapy is effective against primary and advanced uterine cervical cancer, and this preoperative treatment can lead to easier radical hysterectomy. However, further studies are warranted.

12/3,AB/10
DIALOG(R)File 155:MEDLINE(R)
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07643464 93098663 PMID: 1463344
[The pharmacokinetics of intraperitoneal (IP) carboplatin (CBDCA) and dose-up study of intravenous (IV) cyclophosphamide (CPM) in combination with IP CBCDA for advanced ovarian cancer patients]
Fujiwara K; Yamauchi H; Sawada S; Koike H; Mohri H; Ohishi Y; Kohno I Department of Obstetrics and Gynecology, Kawasaki Medical School, Kurashiki, Japan.
Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Dec *1992*, 19 (14) p2373-9, ISSN 0385-0684 Journal Code: 7810034
Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
The pharmacokinetics of IP CBDCA was compared with IV CBDCA and a dose-up study of IV CPM was performed in combination with 400 mg/m2 IP CBDCA for advanced ovarian cancer patients. The maximum concentration of free platinum (F-Pt) in serum following IP CBDCA administration was approximately 1/3 that of F-Pt following IV CBDCA. F-Pt in serum remained more than 90% of total platinum following IP CBDCA until 12 hours after administration. The t1/2 of F-Pt in serum after IP CBDCA administration was two times longer when compared with t1/2 following IV CBDCA, showing the slow peritoneal clearance of CBDCA. The area under curve (AUC) following IP CBDCA was approximately 67% of AUC following IV CBDCA. Cumulative urinary secretion (CUS) of platinum following IP CBDCA was 37% of CUS after IV CBDCA. The maximum tolerable dose of IV CPM in combination with 400 mg/m2 IP CBDCA was 550-600 mg/m2. The dose limiting factor of this combination therapy was *leukocytopenia*. *Thrombocytopenia* was mild in this study. Combination of 400 mg/m2 IP CBDCA and 550-600 mg/m2 seemed to be a tolerable and repeatable therapy for most patients with advanced ovarian carcinoma. Since *thrombocytopenia* was mild and the pharmacokinetics showed the smaller AUC of free platinum in serum following IP CBDCA, a dose-up study for IP CBDCA should be considered.

12/3,AB/11
DIALOG(R)File 155:MEDLINE(R)
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07643462 93098661 PMID: 1463342
[Pharmacokinetics of carboplatin after intraperitoneal administration and clinical effect in ovarian cancer]
Ohno M; Hirokawa M; Hando T

Dept. of Perinato-Gynecology, Kagawa Medical School.
Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Dec *1992*, 19 (14) p2355-61, ISSN 0385-0684
Journal Code: 7810034
Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed

The patients with ovarian cancer are apt to combine peritonitis carcinomatosa (PC). The effect of intraperitoneal (IP) administration of CDDP against peritonitis carcinomatosa was examined. Hydration was not necessary when CBDCA was injected, because nephrotoxicity of CBDCA was very low compared to CDDP. We studied pharmacokinetics of IP-CBCCA and its efficacy and safety. Four hundreds and fifty mg of CBDCA was dissolved in 1,000 ml of saline and administrated through the subcutaneously implanted Infuse-A-Port for 60 minutes. Complete response was 25%. The platinum concentration in the ascites (injected saline) decreased to 90.8 micrograms/ml at 2 hr after administration and to 3.8 micrograms/ml at 24 hrs, and 79.7 97.5% existed as free Pt. The concentration of serous Pt reached to 6.2 micrograms/ml at 15 min. and was kept at 6-8 micrograms/ml. and 52.4-92.7% existed as free Pt in serum. Pt was excreted to urine and reached to the peak concentration at 4 hr. Adverse effect was mainly myelotoxicity without renal toxicity and emesis. *Leukocytopenia* of grade 4 was 14.3%, *thrombocytopenia* was 25.0%. We tried IP administration to the outpatients. The doses were mainly 300 mg, but in some cases, it was escalated to 450 mg, Adverse effect of 300 mg was *thrombocytopenia* of grade 4 (4.8%). These results suggest that IP administration of CBDCA seemed to be a new method as locosystemic chemotherapy. We demonstrated new chemotherapeutic method to outpatients.

12/3,AB/12
DIALOG(R)File 155:MEDLINE(R)
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07585585 93040601 PMID: 1329882
Phase II study of high-dose epirubicin and etoposide in advanced non-small cell lung cancer.
Smit E F; Piers D A; Postmus P E
Department of Internal Medicine, Martini Hospital, Groningen, The Netherlands.
European journal of cancer (Oxford, England - 1990) (ENGLAND) *1992*, 28A (12) p1965-7, ISSN 0959-8049 Journal Code: 9005373 Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

25 consecutive patients with advanced non-small cell lung cancer (NSCLC) were treated with high-dose epirubicin (HDE) 135 mg/m2 and etoposide 60 mg/m2 (days 1-3) every 3 weeks. 121 courses, (median 6, range 1-7), were administered and evaluable for toxicity: WHO grades III/IV *leukocytopenia* in 60/36 (80%) courses, *thrombocytopenia* in 18/6 (20%) and grades II/III anaemia in 31/6 (31%). Median (range) left ventricular ejection fraction (LVEF) fell from 63% (53-73, n = 25) to 60% (48-73 n = 16) after 5 courses (P < 0.02). 2 patients had a drop of more than 15% in LVEF with an epirubicin dose of 675 mg/m2. Apart from 1 patient who had tachycardia 6 months after the last course, no patient had congestive heart failure. There were 2 complete and 7 partial responses [total 9/25 (36%, 95% confidence interval: 18-57.5%)]. Median survival is 31.8 (4.3-75) weeks. Combination HDE and etoposide in NSCLC offers no advantage over HDE alone and is more toxic.

12/3,AB/13
DIALOG(R)File 155:MEDLINE(R)
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07584276 93039280 PMID: 1418307
Rejection associated with early appearance of donor-reactive antibodies after kidney transplantation treated with plasmapheresis and administration of 15-deoxyspergualin. A report of two cases.
Gannedahl G; Ohlman S; Persson U; Gudmundsson S; Larsson E; Tyden G; Totterman T H; Wikstrom B; Weiss L; Groth C G; et al
Department of Transplantation Surgery, University Hospital, Uppsala, Sweden.
Transplant international - official journal of the European Society for Organ Transplantation (GERMANY) Sep *1992*, 5 (4) p189-92, ISSN 0934-0874
Journal Code: 8908516
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

In two kidney transplant patients, one of whom had panel-reactive antibodies (PRA) before transplantation, a pretransplant negative donor-recipient crossmatch became positive within the 1st week after transplantation. Simultaneously, good graft function deteriorated to a state of anuria. One patient graft biopsy showed a vascular rejection, whilst the other patient biopsy was unrevealing. Both patients were treated with plasmapheresis and a new immunosuppressive drug, 15-deoxyspergualin (DSG). Plasmapheresis was performed for 6 and 9 days, respectively, and DSG was given for 5 days in a dosage of 6 mg/kg body weight per day. One of the patients

received methylprednisolone i.v. in addition. During treatment the cross-match became negative and has since remained that way. In both patients the graft function was restored. No adverse effects were seen from the treatment, except for a slight *leukocytopenia* and *thrombocytopenia*.

12/3,AB/14
DIALOG(R)File 155:MEDLINE(R)
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07575971 93030906 PMID: 1329230
Treatment of brain metastases of small cell lung cancer with teniposide. Postmus P E; Smit E F; Berendsen H H; Sleijfer D T; Haaxma-Reiche H Department of Pulmonary Diseases, University Hospital, Groningen, The Netherlands.
Seminars in oncology (UNITED STATES) Apr *1992*, 19 (2 Suppl 6) p89-94, ISSN 0093-7754 Journal Code: 0420432
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Over 50% of patients with small cell lung cancer (SCLC) will develop symptomatic brain metastases during the course of their disease. Results of whole brain radiotherapy, the standard treatment, are rather poor and relapses are frequent. Thus, new modes of therapy are urgently needed for these patients. In this study, the efficacy of teniposide was evaluated at a dose of 150 mg/m2 intravenously on days 1, 3, and 5 at 3-week intervals. In 11 of 26 evaluable patients an intracranial response was observed. Median response duration was 23 weeks (range, 9 to 50). Toxicity was acceptable, with grades 3/4 *leukocytopenia* and *thrombocytopenia* reported in 37% and 16%, respectively, of 123 courses. Therefore, teniposide is an effective agent against brain metastases of SCLC and is suitable for palliation of these patients.

12/3,AB/15
DIALOG(R)File 155:MEDLINE(R)
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07575961 93030896 PMID: 1329226
Phase I study of oral teniposide (VM-26).
Smit E F; Ousterhuis B E; Berendsen H H; Sleijfer D T; Postmus P E Department of Pulmonary Medicine, University Hospital Groningen, The Netherlands.
Seminars in oncology (UNITED STATES) Apr *1992*, 19 (2 Suppl 6) p35-9, ISSN 0093-7754 Journal Code: 0420432
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A phase I study of teniposide administered orally for 5 consecutive days was performed. The first dose was 60 mg/m2/d, with increments of 25 mg/m2/d. Nineteen patients entered the study and received a total of 77 courses with a median of two (range, 1 to 12). Dose-limiting toxicity occurred at 160 mg/m2/d and consisted of myelosuppression, mainly *leukocytopenia*, and gastrointestinal toxicity. Sufficient recovery of blood counts was seen by day 21 to allow for a repeat course. Two patients, treated with teniposide doses of 110 and 160 mg/m2/d, respectively, were considered toxic deaths. Partial alopecia was frequent at doses above 85 mg/m2/d. Retching and vomiting during administration of the drug were encountered in virtually all patients. Oral teniposide 135 mg/m2/d for 5 consecutive days on a 3-week schedule is recommended for evaluation of antitumor efficacy in phase II studies.

12/3,AB/16
DIALOG(R)File 155:MEDLINE(R)
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07575931 93030866 PMID: 1329219
Second-line carboplatin-based chemotherapy for small cell lung cancer: the Groningen experience.
Postmus P E; Smit E F; Berendsen H H; Haaxma-Reiche H
Department of Pulmonary Diseases, University Hospital, Groningen, The Netherlands.
Seminars in oncology (UNITED STATES) Feb *1992*, 19 (1 Suppl 2) p17-23, ISSN 0093-7754 Journal Code: 0420432
Document type: Clinical Trial; Controlled Clinical Trial; Journal Article Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In this report, the results of two phase II studies and one pilot study of second-line carboplatin-based chemotherapy for small cell lung cancer are described. Carboplatin plus vincristine given with or without ifosfamide resulted in response rates of 36% and 53%, respectively, in so-called chemotherapy-resistant patients. Toxicity of the carboplatin/vincristine regimen was mild (hematologic toxicity grade 4 was seen with 13% of the courses), whereas the combination including ifosfamide resulted in grade 4 *thrombocytopenia* in 57% of the courses and grade 4 *leukocytopenia* in 49%. A partial response was seen in one of nine patients with progression of brain metastases after chemotherapy, and in three patients the neurologic function score improved, with minor tumor reduction evident on computed tomography scan

of the brain. We conclude that carboplatin is a useful agent for second-line chemotherapy in patients with an early relapse after induction chemotherapy.

12/3,AB/17
DIALOG(R)File 155:MEDLINE(R)
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07458154 92321695 PMID: 1622146
Tolerance to long-term treatment of malignant midgut carcinoid with a highly purified human leukocyte alpha-interferon.
Ahren B; Engman K; Lindblom A
Department of Surgery, Lund University, Sweden.
Anticancer research (GREECE) May-Jun *1992*, 12 (3) p881-4, ISSN 0250-7005 Journal Code: 8102988
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We report here the long-term toleration of treatment with a highly purified human leukocyte alpha-interferon (Interferon Alfanative) in patients with midgut carcinoid tumours with liver metastases. During an 18-month period, 13 consecutive patients with this diagnosis commenced treatment with a-interferon. Five patients died during the first 2 years of treatment due to tumour progression, and in 2 patients the treatment with a-interferon had to be stopped due to severe adverse effects (mainly joint pain and tiredness). Hence, 6 patients tolerated the treatment for a long-term period (greater than 2 years), and in these patients the treatment has continued for more than 3 years; in 3 of them for more than 4 years. In these 6 patients, adverse effects of mild or moderate degree have been observed in 2 patients: itching and hair loss in one and joint pain and hair loss in another. Except for a significant reduction in the blood number of WBC and thrombocytes (although in no patient did *leukocytopenia* or *thrombocytopenia* develop) and the development of hypothyroidism in one patient, no biochemical tests have shown significant changes during the long-term treatment. In these 6 patients, objective tumour regression has been observed in 2 patients, stable disease in 3 patients and progression in 1 patient. We conclude that, of the patients initiated on treatment with a-interferon for midgut carcinoids with liver metastases, only approximately 50% are still on the treatment after 2 years. These patients, on the other hand, may continue for a longer period of time with a low degree of adverse effects.

12/3,AB/18
DIALOG(R)File 155:MEDLINE(R)
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07433348 92296803 PMID: 1605663
[Phase I study of a new platinum complex 254-S, cis-diammine (glycolato)-platinum (II)]
Ota K; Wakui A; Majima H; Niitani H; Inuyama Y; Ogawa M; Ariyoshi Y; Yoshida O; Taguchi T; Kimura I; et al
Dept. of Internal Medicine, Aichi Cancer Center, Japan.
Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jun *1992*, 19 (6) p855-61, ISSN 0385-0684 Journal Code: 7810034
Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
A new platinum complex 254-S had a superior preclinical therapeutic indices compared to cisplatin, showing decreased renal and gastrointestinal toxicities. Phase I clinical study with a single dose schedule was conducted to investigate the safety, toxicity, pharmacokinetics and possible efficacy against various advanced cancers by a cooperative study of 10 institutions. The drug was administered by i.v. infusion for 60 min dissolved in 250 ml of 5% xylitol solution, without the use of hydration and antiemetics. At least 3 patients at each dose level of 10, 20, 40, 80, 100 and 120 mg/m2 were tested and 28 patients were entered into this study. Myelosuppression, especially *thrombocytopenia*, appeared strongly at dose level of 80 mg/m2 and dose limiting *thrombocytopenia* was found in 2 of 5 patients. *Leukocytopenia* was also dose-related but moderate. Platelet and WBC nadirs occurred around 3 weeks after administration with recovery in about one week. Although slight elevation of BUN and creatinine were temporarily observed in a few cases, no significant renal toxicity was observed. Anorexia, nausea and vomiting were observed in the majority of patients, but milder than cisplatin. In conclusion, 254-S has demonstrated reduced non-hematologic toxicities as compared to cisplatin. This drug appears to be well tolerated and 120 mg/m2 was maximum tolerated dose. The recommended dose for phase II studies was thought to be 100 mg/m2 by i.v. infusion every 4 weeks.

12/3,AB/19
DIALOG(R)File 155:MEDLINE(R)
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07348705 92211864 PMID: 1556844
[Treatment of rejection with deoxyspergualin after renal transplantation] Shinohara Y; Imanishi M; Nishioka T; Uemura T; Kanda H; Matsuura T; Akiyama T;

Kurita T
Department of Urology, Kinki University School of Medicine. Nippon Hinyokika Gakkai zasshi. The japanese journal of urology (JAPAN) Feb *1992*, 83 (2) p236-42, ISSN 0021-5287 Journal Code: 2984841R
Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
Deoxyspergualin (DSG), which is a new immunosuppressive drug developed in Japan, is expected to be an immunosuppressant for the treatment of rejection, because it has immunosuppressive action different from that of other drugs. In the present study we used DSG to treat renal allograft rejection of in total 17 cases; 6 cases with acute rejection, 8 with chronic rejection and 3 with acute on chronic rejection. We infused DSG very slowly over 3 hours at a dose of 3-7 mg/kg/day for 5-7 days. Four cases (44.4%) with acute or acute on chronic rejection showed excellent response to DSG, three cases (33.3%) showed fair response and two cases (22.3%) did not respond at all. We also used DSG in patients with chronic rejection. In many of them, the increase in serum creatinine was suppressed. Ten of the total patients (58.8%) developed side effects including *leukocytopenia*, *thrombocytopenia* , numbness of the fact etc. No patients needed discontinuation of DSG. From the above results, we think that DSG is a safe and effective drug to treat acute rejection. Furthermore, we could get the results which suggest that DSG is effective for the treatment of chronic rejection.

12/3,AB/20
DIALOG(R)File 155:MEDLINE(R)


07343243 92206362 PMID: 1553902
Combination of 5-fluorouracil and recombinant interferon alpha-2B in advanced gastric cancer. A phase I study.
Lee K H; Lee J S; Suh C; Lee Y S; Min Y I; Ahn S H; Park K C; Kim S K; Kim S H
Section of Medical Oncology, University of Ulsan, College of Medicine, Asan Medical Center, Seoul, Korea.
American journal of clinical oncology - the official publication of the American Radium Society (UNITED STATES) Apr *1992*, 15 (2) p141-5, ISSN 0277-3732 Journal Code: 8207754
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Based on recent preclinical data suggesting synergism between 5-fluorouracil (5-FU) and interferon alpha (IFN-alpha) and clinical activity of the combination therapy in colon cancer, 14 patients with advanced gastric cancer were treated with combination therapy of 5-FU and recombinant interferon alpha-2b (rIFN alpha-2b) (Intron A, Schering, Kenilworth, NJ, U.S.A.). The maximum tolerated dose was 5-FU 750 mg/m2/day given as a continuous infusion daily for 5 days followed by weekly bolus injection of the same initial daily dose, plus rIFN alpha-2b 5 X 10(6) U given subcutaneously 3 times weekly starting day 1 of 5-FU infusion. The dose-limiting toxicities were fatigue/weakness, diarrhea, and neurologic toxicities such as somnolence and confusion. The other common side effects were nausea, fever, *leukocytopenia*, *thrombocytopenia*, and the darkening of the skin. Of 13 evaluable patients, 4 had a partial response (duration 6, 14, 24, and 28 weeks). These data suggest that combination therapy of 5-FU plus rIFN alpha-2b is tolerable and has manageable side effects in patients with advanced gastric cancer. Further Phase II study will be needed to define the antitumor activity of this combination.

12/3,AB/21
DIALOG(R)File 155:MEDLINE(R)


07223810 92086314 PMID: 1749582
Ifosfamide, methotrexate and 5-fluorouracil for pretreated advanced breast cancer.
Becher R; Hofeler H; Kloke O; May D; Wandl U; Niederle N; Richter R; Scheulen M E; Schmidt C G
Innere Universitats- und Poliklinik (Tumorforschung), Westdeutsches Tumorzentrum, Essen, BRD.
Oncology (SWITZERLAND) *1991*, 48 (6) p459-63, ISSN 0030-2414 Journal Code: 0135054
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A total of 51 fully evaluable patients with advanced and intensively pretreated breast cancer were treated with a combination chemotherapy of ifosfamide plus mesna, methotrexate and 5-fluorouracil. All patients had received at least one series of combined chemotherapy, 30 patients had received more than one combination and 41 patients had had anthracyclines before. Metastatic lesions in more than one site were found in 42 patients, and 24 patients had metastatic liver lesions. Partial remission was achieved in 10 patients (20%) and no change in 16 patients (31%). Survival was almost identical in both groups of responding patients and significantly shorter in treatment failures. Response was favorable in patients without pretreatment with anthracyclines. Two patients who received this protocol directly after

progression with cyclophosphamide, methotrexate and 5-fluorouracil (CMF protocol) responded with a partial remission. Median time to progression was 7 months for partial responders and 4.5 months for patients achieving a no-change status. Median survival was 8 months for all patients. Toxicity was tolerable. *Leukocytopenia* and *thrombocytopenia* were treatment-limiting parameters. Overall, this protocol is well tolerable and effective in breast cancer patients with advanced disease and in intensively pretreated patients.

12/3,AB/22
DIALOG(R)File 155:MEDLINE(R)
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07214089 92076545 PMID: 1742855
Positive phase II study in the treatment of advanced malignant melanoma with fotemustine.
Schallreuter K U; Wenzel E; Brassow F W; Berger J; Breitbart E W; Teichmann W
Department of Dermatology, University of Hamburg, Federal Republic of Germany.
Cancer chemotherapy and pharmacology (GERMANY) *1991*, 29 (1) p85-7, ISSN 0344-5704 Journal Code: 7806519
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To date, dacarbazine (DTIC) has been the most effective drug in the treatment of advanced metastatic melanoma, achieving response rates of up to 28% (mean, 21%). Multidrug responses were generally no better than those obtained using monotherapy. A quite promising clinical trial was conducted using the new nitrosourea fotemustine. A total of 19 patients presenting with advanced malignant melanoma (clinical stage IV according to the 1987 UICC classification system) underwent treatment involving a more rapid infusion of the drug and a reduction in the rest period from 5 to 3 weeks. This monotherapy with fotemustine yielded two complete responses and seven partial responses; in addition, four patients showed no change and six cases progressed after the induction cycle (median duration of response to date, 7.6 months, including four cases that have not relapsed). Fotemustine was well tolerated by the patients, with the only mild side effects being *thrombocytopenia*, *leukocytopenia* and easily controlled nausea/vomiting. Preclinical studies performed previously indicated that fotemustine inhibits enzymes involved in the ribonucleotide reduction pathway (i.e. DNA synthesis), whereby responding patients (n = 3) appeared to favor the thioredoxin reductase/thioredoxin electron transfer to ribonucleotide reductase, whereas non-responders (n = 4) expressed the alternate glutathione reductase/glutaredoxin mechanism. The 47% response rate obtained in these studies vs the 24% reported previously for fotemustine may reflect variations in enzymes in the ribonucleotide reduction pathway in different patients. However, the efficacy of fotemustine against advanced melanoma warrants more extensive trials of this drug, especially since the quality of life of the patients during and after chemotherapy was not severely affected.

12/3,AB/23
DIALOG(R)File 155:MEDLINE(R)
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07193862 92056225 PMID: 1949371
Combined cisplatin and radiation therapy for advanced bladder cancer. Matsushima M; Tajima M; Kase T; Harada M; Takanami M; Yagishita T; Sawamura Y; Shirai M; Kaneko I; Kuwashima A; et al
Department of Urology, Toho University School of Medicine, Tokyo, Japan. Urologia internationalis (SWITZERLAND) *1991*, 47 Suppl 1 p138-42 , ISSN 0042-1138 Journal Code: 0417373
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Since September 1985, 44 patients with advanced urinary bladder cancer have been treated by combined cisplatin and full-dose radiotherapy. The patients were 32 males and 12 females, and their ages ranged from 33 to 83 years, with a median of 67.4 years. Radiotherapy consisting of a tumor dose of 50-60 Gy was administered with cobalt-60. Cisplatin was infused 5 days at a daily dose of 20 mg on the 1st and 4th weeks of treatment. Of the 39 evaluable patients 27 (69.2%) achieved a complete response. Toxicity was also evaluated for those 44 patients. Mainly gastrointestinal toxicity was noted: loss of appetite in 28 (64%), nausea and/or vomiting in 21 (48%), and diarrhea in 8 (18%). *Leukocytopenia* was noted in 16 (33%) and mild *thrombocytopenia* in 5 (11%). Mild dermatitis was noted in 8 (18%).

12/3,AB/24
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

07140258 92002438 PMID: 1912034
High-dose IgG for neutropenic patients with acquired immunodeficiency syndrome (AIDS).
Salama A; Lohmeyer J; Seeger W; Mueller-Eckhardt C
Department of Internal Medicine, Justus Liebig University Giessen, Federal Republic of Germany.

Annals of hematology (GERMANY) Aug *1991*, 63 (2) p77-8, ISSN 0939-5555 Journal Code: 9107334
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
*Leukocytopenia* and bacterial infections are common and serious complications in patients with AIDS. We report here on three patients in whom the administration of high IgG doses led to gradual (two patients) or prompt (one patient) increases in circulating leukocyte counts (from 200-600 to 2500-5900/microliters), inducing definite improvement in two patients; one patient died from Pneumocystis carinii pneumonia. Although the rise in leukocyte counts lasted for only approximately 3 weeks, high-dose IgG might be a useful therapeutic adjunct in such patients.

12/3,AB/25
DIALOG(R)File 155:MEDLINE(R)


07095710 91336743 PMID: 1831340
[Phase I study of CI-898. CI-898 Study Group]
Taguchi T; Tsukagoshi S; Furue H; Niitani H; Ohta K; Ariyoshi H; Hasegawa K; Majima H; Nakao I; Yasutomi M; et al
Dept. of Surgery, Research Institute for Microbial Diseases, Osaka University.
Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Aug *1991*, 18 (10) p1599-612, ISSN 0385-0684 Journal Code: 7810034
Document type: Clinical Trial; Controlled Clinical Trial; Journal Article ; Multicenter Study ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
We conducted a phase I study of CI-898 (trimetrexate), a new diaminoquinazoline antifolate in 22 patients with solid cancer in a multicenter collaborative study. The dosage schedule was single-dose intravenous administration (single treatment), followed by one or two courses of 5-day intravenous administration (5-day treatment) at 3-week intervals. Starting at 2 mg/m2 (1 n), the dose was increased up to 15 mg/m2 (7.5 n) for single treatment and 12 mg/m2 (6 n) for 5-day treatment. Evaluable cases numbered 18 for single treatment and 17 for 5-day treatment. In single treatment, the highest dose of 15 mg/m2 caused no serious side effect and did not reach the maximum tolerated dose (MTD). In 5-day treatment, *leukocytopenia* and *thrombocytopenia* were found dose dependently, the dose-limiting factor was bone marrow depression, and MTD was 10 mg/m2/day. The leukocyte and platelet counts reached the nadir in 1-3 weeks after initiation of 5-day treatment. The recovery from the nadir required about one week. Subjective side effects included mucitis (mouth, anus), malaise and gastro-intestinal symptoms (nausea, anorexia, diarrhea). None of alopecia, cardiotoxicity and nephrotoxicity were found. In the present phase I study, a tendency of tumor reduction was found in one case each of breast cancer (adenoma) and lung cancer (squamous cell carcinoma). The plasma concentration of the unchanged compound after single treatment showed a biphasic elimination pattern (t1/2 alpha 0.8-1.4 hr, t1/2 beta 9.4-13.0hr). The urinary excretion of the unchanged compound was 14.7-23.5% of the administered dose. In 5-day treatment, no accumulation was found. From the results of the present study, the recommended dosage of CI-898 in the early phase II study was considered to be 8 mg/m2/day intravenously for 5 days (every 3-4 weeks).

12/3,AB/26
DIALOG(R)File 155:MEDLINE(R)


07054471 91295350 PMID: 2067126
An early phase II study of 5-fluorouracil combined with cisplatinum as a second line chemotherapy against metastatic gastric cancer. Ohtsu A; Yoshida S; Saito D; Shimada Y; Miyamoto K; Fujii T; Yoshino M; Yoshimori M
Department of Internal Medicine, National Cancer Center Hospital, Tokyo. Japanese journal of clinical oncology (JAPAN) Apr *1991*, 21 (2) p120-4, ISSN 0368-2811 Journal Code: 0313225
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Twenty-two patients with measurable metastatic gastric cancer, refractory to prior chemotherapy, were treated with a combination chemotherapy of 5-fluorouracil (5FU) and cisdiamminedichroloplatinum (II) (CDDP). 5FU was continuously infused for five consecutive days at a dose of 800 mg/m2/day, and CDDP was given intravenously for five days at a dose of 20 mg/m2/day over 30 min every four weeks. All patients had received only one regimen of prior chemotherapy, and 10 of the 22 had been pretreated with combination of etoposide, doxorubicin and CDDP (EAP). It was possible to evaluate 20 of the 22 patients treated for response and toxicity. Nine of the 20 patients achieved a partial response, the response rate being 45% (23-67% with 95% confidence limits). The nine patients who responded included three who had been pretreated with EAP, indicating that 5FU + CDDP can be used as a second line chemotherapy against gastric cancer, even when the initial intensive chemotherapy, such as EAP, has failed

to obtain or maintain a response. High grade toxicities (WHO grade 3 or 4) of *leukocytopenia*, *thrombocytopenia* and stomatitis were seen in 20, 25 and 40%, respectively. No treatment-related death was, however, observed. The above results suggest that 5FU + CDDP could be promising in a phase II trial with a large number of cases.

12/3,AB/27
DIALOG(R)File 155:MEDLINE(R)
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07032519 91273383 PMID: 1647150
[A phase II study of SM-5887 for advanced gastric cancer] Tsushima K; Sakata Y; Munakata A; Sato T; Chiba Y; Nara H; Kawazu S; Matsukawa M; Ohmi T; Aizawa T; et al
First Dep. of Internal Medicine, Hirosaki University School of Medicine. Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jun *1991*, 18 (7) p1151-4, ISSN 0385-0684 Journal Code: 7810034
Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
A phase II clinical trial of SM-5887, a new totally synthesized anthracycline derivative, was carried out in 13 patients with inoperable or recurrent gastric cancer. No patient had been given anthracycline previously. SM-5887 was administered by I.V. bolus with a dose of 100 mg/m2 every three weeks. Twelve of 13 cases were eligible and evaluable for the response. Of the 12 evaluated cases, 6 showed no change (NC), including one minor response (MR). The remaining 6 cases showed progressive disease (PD). Adverse effects were relatively mild in most cases and included anemia, *leukocytopenia*, *thrombocytopenia* , nausea/vomiting, phlebitis, hair loss and fever. Among them, *leukocytopenia* was observed most frequently.

12/3,AB/28
DIALOG(R)File 155:MEDLINE(R)
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07031760 91272623 PMID: 2053379
[Clinical course of premature and newborn infants of mothers with HELLP syndrome]
Klinische Verlaufe bei Fruh- und Neugeborenen von Muttern mit HELLP-Syndrom.
Nikischin W; Conradt A; Schroder H
Abt. Allgemeine Padiatrie, Universitats-Kinderklinik Kiel. Zeitschrift fur Geburtshilfe und Perinatologie (GERMANY) Jan-Feb *1991*, 195 (1) p16-20, ISSN 0300-967X Journal Code: 0326205 Document type: Journal Article ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed
The HELLP-syndrome is complicated by a maternal mortality of 3.5% and a perinatal mortality between 9.5 and 60%. It is a variant of severe preeclampsia which includes hemolysis, elevated liver enzymes and low platelets. It is described in the literature that neonates of mothers with HELLP-syndrome show characteristic symptoms especially *thrombocytopenia*% *%%, *leukocytopenia* and prenatal somatic dystrophy. In this* *retrospective investigation of 36 preterm and term infants of mothers with* *HELLP-syndrome we found the following results: 1. *Thrombocytopenia** *was seen in 11% and leucocytopenia in 12% of the analysed cases. Anemia was* *seen in 10% of the analysed neonates. They needed transfusion of blood. The* *rate of prenatal somatic dystrophy was increased (58%). 2. Elevated blood* *pressure was observed in 29% of the neonates within the analysed interval.* *The time of artificial ventilation of preterm infants with maternal* *HELLP-syndrome was in 37% extended in comparison with infants without* *HELLP-syndrome in pregnancy. 3. The perinatal mortality was 8%. All* *observed infants during delivery and of the neonatal period in our* *collective survived.*
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* 12/3,AB/29*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06980386 91220904 PMID: 2024552*
* Beneficial treatment with methyl 6-[3-(2-chloroethyl)-3-nitrosoureido]-6-* *deoxy-alpha-D-glucopyranoside in a patient with primary myelofibrosis.* * Asano Y; Shimokawa M; Okabe H; Sanefuji H; Kato K*
* Department of Internal Medicine, Kokura National Hospital, Fukuoka,* *Japan.*
* Acta haematologica (SWITZERLAND) *1991*, 85 (2) p103-4, ISSN* *0001-5792 Journal Code: 0141053*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* We attempted treatment with methyl 6-[3-(2-chloroethyl)-3-nitrosoureido]-* *6-deoxy-alpha-D-glucopyranoside (MCNU), a novel nitrosourea derivative, in* *a 55-year-old man with advanced-stage primary myelofibrosis. MCNU was given* *intravenously at a dose of 50 mg once a month. Following MCNU treatment,* *his anemia and splenomegaly improved markedly. An increased dose of MCNU* *(100 mg, once a month) was even more effective

for relieving the symptoms.* *Severe side effects resulting from this therapy, such as* **leukocytopenia* or *thrombocytopenia*, were never observed. These* *observations indicate that MCNU treatment may be a beneficial management of* *advanced-stage primary myelofibrosis.*
**
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* 12/3,AB/30*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06961510 91201990 PMID: 1826720*
* Chemotherapy for glioblastoma multiforme.*
* Lord J; Coleman E A*
* University of Arkansas for Medical Sciences, College of Nursing, Little* *Rock 72205.*
* Journal of neuroscience nursing - journal of the American Association of* *Neuroscience Nurses (UNITED STATES) Feb *1991*, 23 (1) p68-70,*
*ISSN 0888-0395 Journal Code: 8603596*
* Document type: Journal Article; Review; Review, Tutorial* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Treatment for the patient with a glioblastoma multiforme often includes* *chemotherapy with many specific nursing implications directly associated* *with this form of treatment. While the four agents described share some* *common adverse effects such as nausea and vomiting, even with this* *relatively common adverse effect, the onset, duration and severity varies.* *Multiple other adverse effects like nephrotoxicity, ototoxicity,* **thrombocytopenia* and *leukocytopenia* vary greatly from agent to* *agent in occurrence and severity. Knowing the mode of action for each* *agent, which adverse effects to expect, when to expect them and appropriate* *treatment measures will help the nurse, patient and family to better manage* *these effects and improve quality of life.*
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* 12/3,AB/31*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06952600 91193077 PMID: 2084071*
* Phase II trial of vinblastine in advanced ovarian carcinoma. A* *Gynecologic Oncology Group study.*
* Sutton G P; Blessing J A; Adelson M D; Hanjani P*
* Section of Gynecologic Oncology, Indiana University Medical School,* *Indianapolis.*
* Investigational new drugs (UNITED STATES) Nov *1990*, 8 (4)* * p377-9, ISSN 0167-6997 Journal Code: 8309330*
* Contract/Grant No.: CA 12484; CA; NCI; CA 23501; CA; NCI; CA 27816; CA;* *NCI; +*
* Document type: Clinical Trial; Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* A phase II trial of vinblastine in patients with refractory epithelial* *ovarian adenocarcinoma of the ovary was conducted by the Gynecologic* *Oncology Group (GOG) between March 9, 1988 and July 7, 1988. Vinblastine* *was administered in a dose of 9 mg/m2 intravenously every three weeks until* *disease progression or toxicity supervened. Twenty patients were entered* *initially. One was ineligible due to a previous primary cancer. Thus, 19* *patients are evaluable for toxicity and response. All patients had* *cisplatin-combination chemotherapy and four had prior radiotherapy. Median* *age was 63 years (range 40-75 years). Thirteen patients had disease in the* *pelvis and six had extrapelvic metastases. Ten patients had grade 3 lesions* *and seven had grade 2. A median of two courses (range: 1-6) were* *administered. Toxicity was moderate. Seven patients (36.8%) experienced GOG* *grade 3 or 4* *leukocytopenia* and six had grade 3 or 4* *granulocytopenia. Median nadir WBC was 2,000 cells/microliters (range* *600-3,500) and platelet nadirs for the three patients with* **thrombocytopenia* were 60,000, 116,000, and 147,000. Other toxicity* *included grade 3 gastrointestinal and renal toxicity in one patient each.* *Seven patients (36.8%) had stable disease on therapy and 12 had increasing* *disease. No responses were observed. Vinblastine in this dose and schedule* *is inactive in patients with resistant epithelial ovarian adenocarcinoma* *progressing on first-line chemotherapy.*
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* 12/3,AB/32*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06790183 91029809 PMID: 2171794*
* Phase II study of (glycolate-O,O') diammineplatinum(II), a novel platinum* *complex, in the treatment of non-small-cell lung cancer.* * Fukuda M; Shinkai T; Eguchi K; Sasaki Y; Tamura T; Ohe Y; Kojima A;* *Oshita F; Hara K; Saijo N*
* Department of Internal Medicine, National Cancer Center Hospital, Tokyo,* *Japan.*
* Cancer chemotherapy and pharmacology (GERMANY) *1990*, 26 (6)* * p393-6, ISSN 0344-5704 Journal Code: 7806519*
* Document type: Clinical Trial; Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* A total of 68 patients with non-small-cell lung cancer who either had not* *previously been treated (38) or had undergone prior therapy (30) were* *treated in a

phase II study of (glycolate-O,O') diammineplatinum(II) (NSC* *375 101D; 254-S), a new platinum complex. The drug was given as a single* *intravenous infusion at a dose of 100 mg/m2 every 4 weeks. All 68 patients* *could be evaluated for response and 62, for toxicity. Objective responses* *were seen in 10 of 68 cases (14.7%; 95% confidence interval, 7.3%-25.4%),* *and the median duration of response was 15 weeks (range, 8-23 weeks). The* *response rates were similar for previously untreated and treated patients* *(13% and 17%, respectively), including three previously treated with* *cisplatin. Myelosuppression was the dose-limiting toxicity.* **Thrombocytopenia* (less than 100,000 platelets/mm3) and* **leukocytopenia* (less than 3,000 WBC/mm3) were observed in 22 (35%)* *and 18 (29%) patients, respectively. Mild to moderate nausea and vomiting* *occurred in 45 cases (73%). No significant renal or neurotoxicity was* *observed. We conclude that as a single agent, 254-S is well tolerated but* *appears to have marginal activity against non-small-cell lung cancer.* **

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* 12/3,AB/33*

*DIALOG(R)File 155:MEDLINE(R)*

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*06773883 91013346 PMID: 2145458*

* [Studies on so-called "postoperative erythroderma": report of four cases]* * Kusagawa H; Sato T; Mizumoto T; Mizutani T; Yada I; Yuasa H; Kusagawa M;* *Ichikawa S; Kitade K; Nakamura Y; et al*

* Department of Thoracic and Cardiovascular Surgery, Mie University School* *of Medicine.*

* Kyobu geka. The Japanese journal of thoracic surgery (JAPAN) Sep* **1990*, 43 (10) p783-8, ISSN 0021-5252 Journal Code: 0413533* * Document type: Journal Article ; English Abstract*

* Languages: JAPANESE*

* Main Citation Owner: NLM*

* Record type: Completed*

* Postoperative erythroderma", the pathogenesis of this disease have solved* *as graft-versus-host disease (GVHD) due to blood transfusion, is fatal and* *impossible to cure for the time being. Therefore the prevention against the* *disease is very important. One woman and three men who underwent an* *operation and blood transfusion at our department died of this disease.* *They fell into high fever on 11-13 days, erythroderma on 12-16 days, liver* *dysfunction on 14 days, and *leukocytopenia* on 17-19 days, after* *surgery and transfusion. Eventually, they all suffered from* **thrombocytopenia* , diarrhea, renal dysfunction, and sepsis which led* *to death. The clinical course, macroscopic and microscopic findings of them* *coincided with those of GVHD. Since 1989, we have tried following methods* *for prevention of postoperative erythroderma: Reducing blood transfusion,* *especially fresh blood and fresh thrombocyte plasma, by using predeposited* *autologous blood, autologous washed erythrocytes collected from the* *operative area before and after extracorporeal circulation (ECC),* *concentrated residual blood from the ECC using a hemoconcentrater, and* *1,500 rad of cobalt-irradiation of fresh blood, fresh thrombocyte plasma,* *and blood collected within 7 days prior to the transfusion. Postoperative* *erythroderma has not been experienced by introduction of these methods* *since 1989.*

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* 12/3,AB/34*

*DIALOG(R)File 155:MEDLINE(R)*

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*06773564 91013027 PMID: 1699008*

* [The COP-BLAM therapy for malignant lymphoma]*

* Arai N; Hara A; Umeda M; Shirai T*

* First Department of Internal Medicine, Toho University School of* *Medicine, Tokyo.*

* Rinsho ketsueki The Japanese journal of clinical hematology (JAPAN) Jul* **1990*, 31 (7) p951-7, ISSN 0485-1439 Journal Code: 2984782R* * Document type: Journal Article ; English Abstract*

* Languages: JAPANESE*

* Main Citation Owner: NLM*

* Record type: Completed*

* COP-BLAM therapy, which has recently been reported to be useful in the* *treatment of malignant lymphoma, was performed on 36 patients, and the* *results and adverse effects of treatment were evaluated. Complete remission* *(CR) and partial remission (PR), was obtained in 32 (88.9%) and in 4* *(11.1%) out of the 36 patients, respectively. So the effective ratio was* *100%. Analyzing results according to staging classification, CR was* *obtained in all of those in stages I and II, and in 84% of those in stages* *III and IV. The four patients with recurrent disease after CHOP therapy* *exhibited a CR ratio of 50% indicating that therapy is effective in* *recurrent cases. Adverse effects observed among the patients included* **leukocytopenia* under 1,000/microliters (5.6%), *thrombocytopenia** *under 5 x 10(4)/microliters (2.8%), gastrointestinal symptoms (25%),* *peripheral neuropathy (8.3%) and alopecia (27.3%). The efficacy of COP-BLAM* *therapy appears to be satisfactory with malignant lymphoma, and all adverse* *effects were of mild degree. In addition, it may be effective in the* *treatment of recurrent cases which remitted after CHOP and other therapies.* **

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* 12/3,AB/35*

*DIALOG(R)File 155:MEDLINE(R)*

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*06766370 91005822 PMID: 2209429*

* [Sweet's syndrome after T-lymphoblastic lymphoma and before the* *manifestation of a secondary acute myeloid leukemia]* * Sweet-Syndrom nach T-lymphoblastischem Lymphom und vor der Manifestation* *einer sekundaren akuten myeloischen Leukamie.*
* Ollech-Chwoyka J; Kruger A; Christophers E; Loffler H* * II. Medizinische Klinik und Poliklinik, Universitat Kiel.* * Deutsche medizinische Wochenschrift (GERMANY) Sep 28 *1990*, 115* * (39) p1466-9, ISSN 0012-0472 Journal Code: 0006723* * Document type: Journal Article ; English Abstract*
* Languages: GERMAN*
* Main Citation Owner: NLM*
* Record type: Completed*
* Thirty-two months after the diagnosis and treatment of a T-lymphoblastic* *lymphoma with bone marrow involvement had been made in a 30-year-old* *patient, he developed fever up to 40 degrees C during maintenance treatment* *with methotrexate and 6-mercaptopurine. Later there were tender, blue-red* *skin eruptions, *leukocytopenia* (1.4 x 10(9)/l) and* **thrombocytopenia* (29 x 10(9)/l). Histological examination of a skin* *biopsy revealed acute febrile neutrophilic dermatosis (Sweet's syndrome).* *Bone marrow biopsy revealed hyperplastic myelopoiesis. There was no* *evidence for acute myeloid leukaemia or lymphoma recurrence. After the* *maintenance treatment had been discontinued, treatment with* *methylprednisolone, 60 mg, was begun. The signs of Sweet's syndrome* *regressed, but *thrombocytopenia* and mild *leukocytopenia** *remained. Six months later it was found by morphological and immunological* *tests that he had acute myeloid leukaemia without any chromosomal* *abnormalities. There was still no evidence for a recurrent T-lymphoblastic* *lymphoma.*
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* 12/3,AB/36*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06744294 90370342 PMID: 2168533*
* Pirarubicin in advanced non-small cell lung cancer. A trial of the Phase* *I/II Study Group of the Association for Medical Oncology of the German* *Cancer Society.*
* Drings P; Gunther I U; Gatzemeier U; Berdel W; Stahl M; Salewski E; Edler* *L*
* Abteilung Innere Medizin-Onkologie, Thoraxklinik Heidelberg-Rohrbach,* *FRG.*
* Onkologie (SWITZERLAND) Jun *1990*, 13 (3) p180-4, ISSN* *0378-584X Journal Code: 7808556*
* Document type: Clinical Trial; Journal Article; Multicenter Study* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Forty-seven patients with advanced non-small cell lung cancer (NSCLC)* *were treated in a multicentre phase II study with pirarubicin (THP),* *4'-O-tetrahydropyranyl-doxorubicin using a dosage of 70 mg/m2 every 3* *weeks. The median age of the patients was 59 years (range 45-70) and the* *performance status grade 0-2 (WHO). Thirty-eight patients had stage IV and* *9 stage III (UICC). Twenty-six patients had an adenocarcinoma. 19 a* *squamous cell carcinoma, and 2 a polymorphocellular carcinoma. Six out of* *45 evaluable patients achieved a partial remission leading to an overall* *response rate of 13%. Eighteen patients showed no change (NC), 12 were* *progressive (PD), 2 patients had early progression (EP), and 7 patients* *died during the first course with clinical signs of tumor progression* *(early death). The median survival time was 4.6 months.* **Leukocytopenia* and *thrombocytopenia* (WHO grade 4) was* *experienced in 8.5% and 2.1%, nausea and vomiting (grade 2 and 3) by 32% of* *the patients. There was no cardiotoxicity or other severe side effects.* *Pirarubicin has only a moderate antineoplastic activity in patients with* *advanced NSCLC. Observed response rates are similar to those reported for* *doxorubicin, but the toxic side effects are milder.*
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* 12/3,AB/37*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06744293 90370341 PMID: 2204003*
* Phase II study of pirarubicin in metastatic breast cancer.* * Kleeberg U R; Reichel L; Wander H E; Beyer J H; Essers U; Fiebig H H;* *Salewski E; Greifenberg B; Edler L*
* Hamatologisch-Onkologische Praxis Altona, Hamburg, FRG.* * Onkologie (SWITZERLAND) Jun *1990*, 13 (3) p175-9, ISSN* *0378-584X Journal Code: 7808556*
* Document type: Clinical Trial; Journal Article; Multicenter Study* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Pirarubicin is a more lipophilic derivative of doxorubicin, with a higher* *uptake rate of cells, lower cardiotoxicity and better antitumor efficacy in* *preclinical models. Thirty-four patients with metastatic breast cancer were* *treated in a multicenter phase II study with pirarubicin (THP) using a* *dosage of 75 mg/m2/every 3 weeks. The patients had a median age of 56 years* *(range 41-73) and a performance status of WHO grade 0-2. Patients* *pretreated with anthracyclines, or who were older than 75 years and without* *sufficient bone marrow reserve were

excluded. The 32 evaluable patients* *received a median number of 4 cycles (range 2-8). The myelosuppression was* *dose-limiting and led to infections (grades 1 and 2) in 5 patients.* *Twenty-eight patients developed *leukocytopenia* grade 3 and 4 toxicity* *and 7 patients experienced *thrombocytopenia* grade 1 and 2. The drug* *was subjectively well tolerated and nausea, vomiting and alopecia were* *mild. One complete remission with a duration of 15.4 months (67 weeks) and* *7 partial remissions with a median duration of 9.3 months (40 weeks) were* *achieved, which resulted in an overall response rate of 25%. Twenty-one* *patients were stable for 17 weeks (median) under the treatment with* *pirarubicin.*
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* 12/3,AB/38*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06726453 90352490 PMID: 2386894*
* A phase II study of pirarubicin in malignant pleural mesothelioma.* * Kaukel E; Koschel G; Gatzemeyer U; Salewski E*
* Pulmonary Department, General Hospital, Hamburg, FRG.* * Cancer (UNITED STATES) Aug 15 *1990*, 66 (4) p651-4, ISSN* *0008-543X Journal Code: 0374236*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Thirty-five non-pretreated patients (29 male, six female) with malignant* *pleural mesothelioma, median age of 68.5 years (range, 29 to 78 years) and* *a median performance status of 80% (range, 60% to 100%) were treated with* *70 mg/m2 Pirarubicin. The treatment was repeated every 3 to 4 weeks (median* *duration per cycle, 23 days) up to progression or severe toxicity. The* *median cumulative dose given was 294 mg/m2, or 4.5 cycles. All patients* *were evaluable regarding response. Three partial remissions were achieved,* *leading to a remission rate of 8.6%. The median duration of remission was 6* *months. Five patients achieved minor response, and a further 14 patients* *were stable under treatment with Pirarubicin. The median survival time was* *10.5 months. *Leukocytopenia* was the main dose-limiting factor and 20*% *of the patients experienced World Health Organization (WHO) Grades III and* *IV. Anemia and *thrombocytopenia* were mild. Nausea and vomiting, WHO* *Grades I and II, were observed in 46% of all patients. Alopecia, Grades I* *and II, was seen in 47% and Grade III in 6%. No signs of cardiac* *dysfunction were detectable, except for cardiac arrhythmia in four patients* *(11%). Pirarubicin is an active drug in the treatment of pleural* *mesothelioma with fewer severe side effects than doxorubicin.* **
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* 12/3,AB/39*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06648755 90274440 PMID: 2190537*
* Efficacy of Cepharanthin for preventing leukopenia and* **thrombocytopenia* induced by chemotherapy in breast cancer* *patient--prospective randomized study]*
* Suzuki S; Abe R; Nihei M; Kimijima I; Tsuchiya A; Nomizu T* * 2nd Dept. of Surgery, Fukushima Medical College.*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jun *1990*, 17* * (6) p1195-200, ISSN 0385-0684 Journal Code: 7810034* * Document type: Clinical Trial; Journal Article; Randomized Controlled* *Trial ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* A prospective randomized study was carried out to evaluate the efficacy* *of Cepharanthin (CEP) on *leukocytopenia* and *thrombocytopenia** *during chemotherapy in breast cancer patients. The CEP group (51 patients)* *was administered CEP by 60 mg/day p.o.. The control group (55 patients) was* *not administered CEP in all the times. The rate of *leukocytopenia* was* *significantly lower (p less than 0.05) in the CEP group than in the* *control. But the recovery periods from nadir to normal range in WBC were* *not significantly different between the two groups. The average of nadir of* *WBC in the *leukocytopenia* patients was higher in the CEP group than* *in the control, but it was not significant. In MMVC group and MMC + TAM* *group, the rate of *leukocytopenia* was significantly lower in the CEP* *group than in the controls. The obvious efficacy of CEP for* **thrombocytopenia* was not obtained in this study. We conclude that CEP* *showed an efficacy on preventing *leukocytopenia* induced by* *chemotherapy in breast cancer patients.*
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* 12/3,AB/40*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06596190 90221541 PMID: 2326057*
* [Hematologic changes in sarcoidosis]*
* Haematologiai elteresek sarcoidosisban.*
* Vezendi S; Dobran I*
* Debreceni Orvostudomanyi Egyetem, Sziv- es Tudogyogyaszati Klinika.* * Orvosi hetilap (HUNGARY) Apr 1 *1990*, 131 (13) p679-81, ISSN* *0030-6002 Journal Code: 0376412*
* Document type: Journal Article ; English Abstract*

* Languages: HUNGARIAN*
* Main Citation Owner: NLM*
* Record type: Completed*
* On the basis of the literature authors analyse the importance of the* *involvement of spleen in sarcoidosis and the haematological changes that* *follow from this. In a group of patients with sarcoidosis of their own* *department (more than 1200 patients) they observed 2 women with* *thrombocytopenic purpura, one woman with thrombo- and *leukocytopenia*,* *and one woman with agranulocytosis. They shortly reviewed the previous* *history of their patients, the disease process, and the results of the* *treatment. All the four of their patients were given corticosteroid* *treatment and with this the *thrombocytopenia* was cured. No relapse* *was observed. One of the patients they have followed for 25 years, and an* *other one for 20 years. The patient with agranulocytosis was given* *corticosteroid, granulocyte concentrate, gammaglobulin, and antibiotics,* *too. Her status also became settled, and during the 10 years after her* *first observation we did not notice any relapse. The fourth patient is* *still being treated.*
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**
* 12/3,AB/41*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06493694 90118607 PMID: 2481928*
* Advanced mycosis fungoides: chemotherapy with etoposide, methotrexate,* *bleomycin, and prednimustine.*
* Doberauer C; Ohl S*
* Department of Internal Medicine, University of Essen, Federal Republic of* *Germany.*
* Acta dermato-venereologica (SWEDEN) *1989*, 69 (6) p538-40,* *ISSN 0001-5555 Journal Code: 0370310*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* We assessed the efficacy and toxicity of a chemotherapeutic regimen in* *patients with stage II-IV mycosis fungoides. Eleven previously treated* *outpatients received etoposide and methotrexate p.o. and bleomycin i.v.* *every 3 weeks. There was 1 complete remission for 2 months and 7 partial* *remissions with a median duration of 6 months (range 2-16 months). Three* *patients showed stable disease lasting 1-5 months (median 2 months). In 4* *patients, remissions were maintained with prednimustine after 10 courses of* *induction chemotherapy. Mild nausea occurred in all patients and severe* **leukocytopenia* and *thrombocytopenia* in 1 patient. Toxicity of* *the treatment regimen was acceptable and response rates comparable to those* *seen by others with more toxic single-agent or combination chemotherapies.* **
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* 12/3,AB/42*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06448638 90073334 PMID: 2480104*
* Induction chemotherapy with cisplatinum, 5-fluorouracil, bleomycin,* *mitomycin C and hydroxyurea for previously untreated locally advanced* *squamous cell carcinomas of the head and neck.*
* Fountzilas G; Nicolaou A; Sridhar K; Sideras T; Haritanti A; Anastasakis* *C; Delis V; Vritsios A; Daniilidis J*
* Department of Medicine, AHEPA University Hospital, Thessaloniki, Greece.* * Archives of oto-rhino-laryngology (GERMANY, WEST) *1989*, 246 (5)* * p373-7, ISSN 0302-9530 Journal Code: 0414105*
* Document type: Clinical Trial; Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Fifty-three patients with locally advanced squamous cell carcinoma of the* *head and neck (SCCHN) were treated with a combined modality treatment* *consisting of three cycles of induction chemotherapy before definitive* *surgery and/or radiotherapy. Two additional cycles of the same chemotherapy* *were given after local-regional therapy. The chemotherapeutic regimen* *included cisplatinum 100 mg/m2 on day 1, 5-fluorouracil 1000 mg/m2 as a* *continuous infusion on days 2-6, bleomycin 15 units i.m. on days 15 and 29,* *mitomycin C 4 mg/m2 i.v. on day 22 and hydroxyurea 1000 mg/m2 p.o. on days* *23-27. Each cycle was repeated every 42 days. Forty-nine patients are* *evaluable for response. There were 37 men and 12 women, with a median age* *of 58 years (range 18-75 years) and performance status of 80 (range 40-90).* *Sixteen patients (33%) demonstrated a complete response, 20 (41%) a partial* *response, yielding a 74% response rate to induction chemotherapy; 12 (24%)* *patients had stable disease and 1 (2%) progressive disease. The actuarial* *survival of those patients who completed the whole treatment program was* *65% at 2 years and 47% at 3 years. Toxicities included nausea and vomiting* *(66%). anemia (34%), *leukocytopenia* (54%), *thrombocytopenia** *(22%), stomatitis (36%), diarrhea (10%), alopecia (78%), hear impairment* *(4%) and transient creatinine elevation (2%). The results of the present* *study showed that induction chemotherapy with the above regimen produced a* *high rate of complete responses and can be safely combined with* *local-regional therapy to improve local tumor control and increase* *disease-free survival in patients with locally advanced SCCHN.* **

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* 12/3,AB/43*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06405700 90030220 PMID: 2804978*
* Toxicity of methotrexate in rats preexposed to nitrous oxide.* * Ermens A A; Schoester M; Spijkers L J; Lindemans J; Abels J* * Institute of Hematology, Erasmus University Rotterdam, The Netherlands.* * Cancer research (UNITED STATES) Nov 15 *1989*, 49 (22) p6337-41,* *ISSN 0008-5472 Journal Code: 2984705R*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Several chemotherapeutic protocols for the treatment of malignancies* *include administration of methotrexate (MTX) during or shortly after total* *anesthesia. Clinical observations in patients treated for breast carcinoma* *or childhood cancer have shown unexpected myelosuppression and mucosal* *damage. This phenomenon may be attributed to the synergistic effects of* *nitrous oxide, which inactivates the cobalamin coenzyme of methionine* *synthase, and MTX, which inhibits dihydrofolate reductase, on folate* *metabolism. However, no quantitative data on dose-effect relationships are* *available regarding the combined toxicity of MTX and N2O. We investigated* *the effect of exposure to N2O on the toxicity of MTX. Groups of male Wistar* *rats were exposed to either 50% N2O/50% O2 or air for 12-48 h.* *Subsequently, a single i.p. injection of 10, 20, 40, or 80 mg MTX/kg body* *weight was given. Gastrointestinal toxicity resulted in diarrhea and weight* *loss in all groups for 5 days after MTX administration. Concomitantly, bone* *marrow depression with *leukocytopenia* and *thrombocytopenia** *occurred. Exposure to N2O did not alter the plasma clearance of MTX. No* *substantial liver or kidney toxicity could be detected, but the 50% lethal* *dose for MTX was reduced from 60 mg/kg to 10 mg/kg if rats had been exposed* *to N2O for 48 h; the main causes of death were dehydration and bleeding.* *The administration of 5-formyl-tetrahydrofolate (4 x 10 mg i.p.) but not* *5-methyltetrahydrofolate protected completely against the lethal effect of* *the drug combination. Altogether, cytotoxic effects of MTX on proliferating* *cells are potentiated by N2O. Therefore, the use of this anesthetic shortly* *before or during MTX administration should be avoided.* **
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* 12/3,AB/44*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06398900 90023334 PMID: 2801602*
* Induction chemotherapy with cisplatin and continuous infusion* *5-fluorouracil in locally far-advanced head and neck cancer.* * Verweij J; de Jong P C; de Mulder P H; van der Broek P; Alexieva-Figusch* *J; van Putten W L; Schornagel J H; Ravasz L A; Snow G B; Vermorken J B* * Department of Medical Oncology, Rotterdam Cancer Institute, The* *Netherlands.*
* American journal of clinical oncology - the official publication of the* *American Radium Society (UNITED STATES) Oct *1989*, 12 (5) p420-4,* *ISSN 0277-3732 Journal Code: 8207754*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Induction combination chemotherapy with cisplatin, 100 mg/m2 i.v. day 1,* *and 5-fluorouracil, 1,000 mg/m2/24-h infusion days 1-4, was applied in 76* *patients with locally far advanced squamous-cell cancer of the head and* *neck. The treatment program consisted of 3 cycles of chemotherapy, followed* *by local radiotherapy and/or surgery. Hematologic side effects were* **leukocytopenia* (50%) and *thrombocytopenia* (35%). Other side* *effects included renal toxicity (23%), nausea and/or vomiting (86%),* *alopecia (18%), and phlebitis (45%). Thirteen patients (17%) achieved a* *complete remission and 37 patients (49%) a partial remission. Median* *progression-free and overall survival were 8 and 11 months, respectively.* *Only patients achieving a complete remission had a better prognosis.* *Although induction chemotherapy may facilitate further local treatment in* *about half of the patients, on the basis of presently available data, this* *procedure should not be routinely applied with the aim of better survival.* **
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* 12/3,AB/45*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06380946 90005339 PMID: 2676498*
* Hematotoxicity and carcinogenicity of benzene.*
* Aksoy M*
* Research Institute for Basic Sciences, Department of Biology, Gebze,* *Kocaeli, Turkey.*
* Environmental health perspectives (UNITED STATES) Jul *1989*, 82* * p193-7, ISSN 0091-6765 Journal Code: 0330411*
* Document type: Journal Article; Review; Review, Tutorial* * Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The hematotoxicity of benzene exposure has been well known for a century.* *Benzene causes *leukocytopenia*, *thrombocytopenia*, pancytopenia,* *etc. The clinical and hematologic picture of aplastic anemia resulting from*

*benzene exposure is not different from classical aplastic anemia; in some* *cases, mild bilirubinemia, changes in osmotic fragility, increase in lactic* *dehydrogenase and fecal urobilinogen, and occasionally some neurological* *abnormalities are found. Electromicroscopic findings in some cases of* *aplastic anemia with benzene exposure were similar to those observed by* *light microscopy. Benzene hepatitis-aplastic anemia syndrome was observed* *in a technician with benzene exposure. Ten months after occurrence of* *hepatitis B, a severe aplastic anemia developed. The first epidemiologic* *study proving the leukemogenicity of benzene was performed between 1967 and* *1973 to 1974 among shoe workers in Istanbul. The incidence of leukemia was* *13.59 per 100,000, which is a significant increase over that of leukemia in* *the general population. Following the prohibition and discontinuation of* *the use of benzene in Istanbul, there was a striking decrease in the number* *of leukemic shoe workers in Istanbul. In 23.7% of our series, consisting of* *59 leukemic patients with benzene exposure, there was a preceding* *pancytopenic period. Furthermore, a familial connection was found in 10.2*% *of them. The 89.8% of our series showed the findings of acute leukemia. The* *possible factors that may determine the types of leukemia in benzene* *toxicity are discussed. The possible role of benzene exposure is presented* *in the development of malignant lymphoma, multiple myeloma, and lung* *cancer.*
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* 12/3,AB/46*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06375035 89391507 PMID: 2506834*
* [Effects of prophylactic intraportal chemotherapy on liver function,* *blood profile and survival in patients with colo-rectal cancer]* * Inoue Y; Sawada T; Shimizu T; Ishiguro M; Wakatsuki T; Hamazoe R; Shimizu* *N; Maeta M; Koga S*
* First Dept. of Surgery, Tottori University College of Medicine.* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Aug *1989*, 16* * (8 Pt 2) p3024-7, ISSN 0385-0684 Journal Code: 7810034* * Document type: Clinical Trial; Journal Article; Randomized Controlled* *Trial ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Postoperative intraportal anti-cancer chemotherapy was used for 51* *patients with curatively resected colorectal cancer who were selected in* *the randomized controlled study to evaluate its inhibitory effect on liver* *metastasis from colo-rectal cancer. In cases of intraportal chemotherapy,* *30 mg of Mitomycin-C (in 3 doses) and 5 mg/kg (B.W.)/day (1985-1986) or 3* *mg/kg/day (1987-1988) of 5-FU was injected through the catheter inserted* *into the portal vein during postoperative 14 days. In cases of the control* *group (58 patients), the same doses of the drugs were injected into the* *peripheral vein during the same term. Six patients with recurrences were* *observed in the intraportal chemotherapy group, and 3 of them had liver* *metastases. In the control group, more liver metastases were observed (5 of* *7 recurrences were liver metastases). Intraportally injected 5 mg/kg/day of* *5-FU slightly disturbed the liver function. The averages of the serum GOT,* *GPT and gamma-GTP level of these cases were higher than those of the* *control cases. Three mg/kg/day of intraportally injected 5-FU had no* *influence on the liver function. There were no differences in the incidence* *of *leukocytopenia* or *thrombocytopenia* between the two groups.* **
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* 12/3,AB/47*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06375032 89391504 PMID: 2782905*
* [Intra-arterial infusion chemotherapy of advanced breast cancer--effects* *and side effects of adriamycin, 4'-epi-adriamycin and THP-adriamycin]* * Toda K; Asaishi K; Okazaki M; Okazaki Y; Okazaki A; Sato H; Mikami T;* *Watanabe Y; Hayasaka H; Narimatsu E*
* First Dept. of Surgery, Sapporo Medical College.*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Aug *1989*, 16* * (8 Pt 2) p3011-4, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* In 34 patients with primary advanced breast cancer, intra-arterial* *administration of ADR (50 mg X 3, total dose 150 mg, 10 cases), 4' epi ADR* *(50 mg X 3, 150 mg, 8 cases; 70 mg X 3, 210 mg, 10 cases) and THP-ADR (50* *mg X 3, 150 mg, 6 cases) was performed, and its effects and side effect* *were analyzed. The clinical and histological response rate were superior in* *the ADR (150 mg) regimen and 4'-epi-ADR (150 mg) regimen. Signs of systemic* *toxicity such as gastrointestinal disorders, *leukocytopenia* and* **thrombocytopenia* were the side effects in patients treated with* *THP-ADR, but the frequency of alopecia was lower. No cardiotoxicity was* *recorded in any of the patients. These results indicated that 4'-epi-ADR* *given the total dose of 150 mg in a single dosage of 50 mg was the most* *effective agent in intra-arterial infusion chemotherapy for advanced breast* *cancer.*
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* 12/3,AB/48*

*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06305418 89321573 PMID: 2502072*
* [Vincristine, adriamycin, mitomycin-C and UFT (VAM-UFT) therapy in* *progressive or recurrent breast cancer]*
* Yasutake K; Imamura Y; Yoshimura Y; Oya M; Matsushita K; Hozumi T; Katou* *J; Okutani T; Irie K*
* Hyogo Medical Center for Adults, Dept. of Gastroenterology* *(Gastrointestinal Internal Medicine).*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jul *1989*, 16* * (7) p2373-9, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Since June 1984, 23 cases of progressive or recurrent breast cancers were* *treated with combination chemotherapy of VAM-UFT consisting of vincristine,* *adriamycin, mitomycin C and UFT. Clinical effects of VAM-UFT therapy were 3* *CR, 12 PR, and the response rate was 65.2%. Its effective interval was 3* *months. But the patients treated with over 4 cycles of VAM-UFT therapy* *showed an 85% response rate, with a 5-month effective interval. In each* *patient's background, a shorter disease free interval tended to be more* *highly effective, but other factors were not significant. Scirrhous* *carcinoma of pathology evidenced slightly high response rate. Compared with* *the survival time of patients treated with under 3 cycles and over 4 cycles* *of this therapy, the latter was significantly longer. Toxicity involved* **leukocytopenia* (74%), *thrombocytopenia* (22%), anemia (30%),* *alopecia (91%), nausea and vomiting (87%) and stomatitis (35%), but cases* *in which the treatment was stopped were not observed. Therefore VAM-UFT* *therapy had a highly therapeutic effect, reflected in an 85% response rate,* *for progressive or recurrent breast cancers.*
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* 12/3,AB/49*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06272512 89288569 PMID: 2661049*
* Plasma proteolysis and circulating cells in relation to varying endotoxin* *concentrations in porcine endotoxemia.*
* Naess F; Roeise O; Pillgram-Larsen J; Ruud T E; Stadaas J O; Aasen A O* * Department of Surgery, Ulleval Hospital, University of Oslo, Norway.* * Circulatory shock (UNITED STATES) Jun *1989*, 28 (2) p89-100,* *ISSN 0092-6213 Journal Code: 0414112*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Ten juvenile pigs receiving a continuous infusion of 0.01 mg/kg of* *endotoxin over 3 hr and seven animals infused with sterile saline (serving* *as controls) were studied for 5 hr. Endotoxin concentrations in plasma as* *determined with a chromogenic Limulus amoebocyte lysate (LAL) test reached* *a steady state of about 1,000 ng/liter after 1 hr and declined rapidly as* *the infusion was discontinued. Preinfusion values were reached at the end* *of the observation period. Endotoxin concentrations found during the* *infusion period were comparable with those seen in humans with septicemia.* *The endotoxin infusion was followed by hemoconcentration,* **leukocytopenia*, and *thrombocytopenia*. Using chromogenic peptide* *substrate assays, activation of the plasma kallikrein-kinin, fibrinolytic,* *and coagulation systems was detected. Although the endotoxin concentrations* *reached preinfusion values within the last 2 hr of the observation period,* *changes found in circulating cells and components of the plasma cascade* *systems did not normalize, and the hemodynamic situation did not change.*
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* 12/3,AB/50*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06220976 89236711 PMID: 2716202*
* [Severe aplastic anemia remarkably improved by a treatment with* *antilymphocyte globulin, high-dose methylprednisolone and danazol]* * Miyamura K; Kojima S; Takeyama K; Matsushita T; Minami S; Kodera Y* * Rinsho ketsueki The Japanese journal of clinical hematology (JAPAN) Jan* **1989*, 30 (1) p72-7, ISSN 0485-1439 Journal Code: 2984782R* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Sixteen-years-old female with severe aplastic anemia received a therapy* *combined with antilymphocyte globulin (ALG), high-dose methylprednisolone* *(m-PSL) and danazol. At the hospitalization, hematological examination* *demonstrated as follows; reticulocyte 21,000/microliters, granulocyte* *350/microliters, platelet 10,000/microliters and hypocellular bone marrow.* *Treatment schedule were 1) m-PSL 1,000 mg (day 1-4), 500 mg (5-8)--then* *tapered. 2) ALG lg/day (day 4-8) 3) danazol 600 mg/day. During ALG* *administration, *leukocytopenia* and *thrombocytopenia* appeared* *but thereafter hematological recovery was obtained and the patient was free* *from supportive care. She developed mild diabetes mellitus and moderate* *liver dysfunction,

nevertheless, both of which were controlled. At 3 months* *after the beginning of the treatment, hematological examination* *demonstrated as follows; reticulocyte 236,000/microliters, granulocyte* *1,900/microliters, platelet 56,000/microliters and normocellular bone* *marrow. Although this immunosuppressive therapy was remarkably effective to* *this patient, immunological relation to the onset of aplastic anemia was* *not demonstrated in in vitro examination. This combined therapy seems to be* *effective one for patients with severe aplastic anemia.* **

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* 12/3,AB/51*

*DIALOG(R)File 155:MEDLINE(R)*

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*06219968 89235702 PMID: 2715807*

* A phase I pharmacokinetic study of 21-day continuous infusion* *mitoxantrone.*

* Greidanus J; de Vries E G; Mulder N H; Sleijfer D T; Uges D R; Oosterhuis* *B; Willemse P H*

* Department of Internal Medicine, University Hospital, Groningen, The* *Netherlands.*

* Journal of clinical oncology - official journal of the American Society* *of Clinical Oncology (UNITED STATES) Jun *1989*, 7 (6) p790-7,* *ISSN 0732-183X Journal Code: 8309333*

* Document type: Journal Article*

* Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* A phase I study of mitoxantrone given as a continuous infusion for 21* *days using a venous access port and a portable pump was performed. The* *first dose step was 0.3 mg/m2/d for 21 days. Courses were repeated every 6* *weeks. Dose increment per step was 0.1 mg/m2/d in the first three dose* *steps and 0.2 mg/m2/d in the latter dose steps. Twenty-five patients* *entered the study and received a total of 50 courses, with a median of two* *courses (range, one to five). Up to 0.5 mg/m2/d, no toxicity (according to* *the World Health Organization [WHO] criteria) occurred. At 0.7 mg/m2/d, one* *patient experienced grade 2 *leukocytopenia* and at the 0.9 mg/m2/d* *dose step, one patient experienced grade 2 *leukocytopenia*, grade 1* **thrombocytopenia* , and grade 1 hair loss. At 1.1 mg/m2/d, two of six* *patients had grade 3 *leukocytopenia*, and in one patient treatment was* *discontinued after two days because of myocardial infarction. In both* *patients receiving 1.3 mg/m2/d, treatment was discontinued after 2 weeks* *because of grade 3 *leukocytopenia*. Three patients at the 1.1 mg/m2/d,* *dose step and two patients at the 1.3 mg/m2/d dose step experienced some* *nausea in the last week of the infusion period. One patient developed* *subclavian vein thrombosis. No infectious complications occurred.* *Pharmacokinetic studies were performed by high-performance liquid* *chromatography (HPLC) with ultraviolet (UV) detection. Plasma steady-state* *was reached after 35 hours. During steady-state there was a linear* *relationship between the mitoxantrone dose administered and the level of* *mitoxantrone in plasma (r = .93, P less than .005). The mitoxantrone level* *in leukocytes increased significantly during the infusion period at the 0.9* *mg/m2, the 1.1 mg/m2, and the 1.3 mg/m2 dose steps. The area under the* *curve (AUC) in leukocytes was higher with continuous infusion of 1.1* *mg/m2/d for 21 days compared with bolus injection of 12 mg/m2. Mitoxantrone* *could be detected in plasma for at least five days after the end of the* *21-day infusion period and in leukocytes for at least 14 days. Continuous* *infusion mitoxantrone may increase intracellular drug uptake as expressed* *by intracellular AUC. We recommend a dose of 1.1 mg/m2/d for 3 weeks for* *evaluation of antitumor efficacy in phase II studies.* **

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* 12/3,AB/52*

*DIALOG(R)File 155:MEDLINE(R)*

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*06203703 89219339 PMID: 2710232*

* [Diagnosis and treatment of malignant histiocytosis]* * Diagnostiek en behandeling van maligne histiocytose.* * Sonneveld P; van Lom K; Prins M E; Kappers-Klunne M C; Abels J* * Nederlands tijdschrift voor geneeskunde (NETHERLANDS) Mar 11 *1989** *, 133 (10) p510-4, ISSN 0028-2162 Journal Code: 0400770* * Document type: Journal Article ; English Abstract*

* Languages: DUTCH*

* Main Citation Owner: NLM*

* Record type: Completed*

* Of twelve patients with malignant histiocytosis admitted between 1974 and* *1987, clinical symptoms, diagnostic procedures and the course of the* *disease were retrospectively evaluated. Predominant findings at physical* *examination were fever (11/12), splenomegaly (12/12), hepatomegaly (8/12),* *and lymphadenopathy (8/12). Laboratory findings included anaemia,* **leukocytopenia*, *thrombocytopenia* , high lactate dehydrogenase,* *and jaundice. Positive diagnostic procedures included biopsies or aspirates* *of bone marrow (11/12), spleen (6/10), liver (7/9), lymph node (4/4), skin* *(1/2), lung (1/1) and blood (2/12). In seven patients treated with* *combination chemotherapy an average survival of 540 days was observed,* *while two long-term disease-free survivals were accomplished.* **

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* 12/3,AB/53*

*DIALOG(R)File 155:MEDLINE(R)*

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*06142297 89157709 PMID: 2493527*

* [UFT/CDDP treatment in advanced gastric cancer--case report]* * Suga S; Nagai H; Horiuchi Y; Ohkita T; Ibayashi J; Koyama Y* * Dept. of Gastroenterology, National Nagoya Hospital.* * Gan no rinsho. Japan journal of cancer clinics (JAPAN) Jan *1989*,* * 35 (1) p87-92, ISSN 0021-4949 Journal Code: 1257753* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* In treating advanced gastric cancer cases, 100 mg/m2 of cisplatin (CDDP)* *was given to such patients by means of a 24 hr continuous iv infusion once* *a month. This was in addition to daily UFT chemotherapy with an oral* *administration of UFT at a dose of 200 mg/m2 twice a day before meals. In* *this paper, two patients who achieved an objective tumor response to this* *UFT/CDDP chemotherapy are discussed. It was felt that this treatment was* *not likely to induce either *leukocytopenia* or *thrombocytopenia*.* *With regard to this drug combination, it has been reported that a* *remarkable, synergistic, antitumoral activity of combined 5-fluorouracil* *and cisplatin was demonstrated against L-1210 leukemia in BDF1 mice.* **
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* 12/3,AB/54*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*06128513 89143864 PMID: 2645533*
* Secondary hypersplenism due to Caroli syndrome complicating* *immunosuppression in a renal allograft recipient.*
* Watschinger B; Schwaighofer B; Wrba F; Pohanka E; Kovarik J* * Department of Medicine II, University of Vienna, Austria.* * Nephron (SWITZERLAND) *1989*, 51 (3) p413-5, ISSN 0028-2766* *Journal Code: 0331777*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The differential diagnosis of *thrombocytopenia* and* **leukocytopenia* in renal allograft recipient can be troublesome. We* *report on a patient in whom the rare case of portal hypertension with* *secondary hypersplenism due to Caroli syndrome was detected to be the cause* *for the hematological disturbance. The management of the thereby* *complicated immunosuppressive regimen is discussed.*
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* 12/3,AB/55*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05828578 88182285 PMID: 2451473*
* [Hepatic artery infusion chemotherapy with cisplatin and adriamycin in* *combination with angiotensin-II in the treatment of malignant liver tumors]* * Morita S; Matsumoto S; Odani R*
* Dept. of Radiology, Kochi Municipal Central Hospital.* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Apr *1988*, 15* * (4 Pt 1) p689-95, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Hepatic arterial infusion chemotherapy with cisplatin (CDDP) and* *adriamycin (ADR) in combination with angiotensin-II (AT-II) was performed* *in 19 cases of hepatocellular carcinoma (HCC), 16 cases of metastatic liver* *tumor (MLT) and one case of cholangiocellular carcinoma. CDDP (60-120 mg)* *and ADR (20-50 mg) were infused into the hepatic artery with intra-arterial* *instillation of AT-II (0.5-1.5 microgram/min). Transcatheter arterial* *embolization (TAE) was additionally performed in 10 cases of HCC and 3* *cases of MLT. The response rates for infusion chemotherapy combined with* *TAE were 44% in HCC and 67% in MLT. On the other hand, the response rates* *without TAE were 0% in HCC and 42% in MLT. In some cases of HCC, however, a* *marked decrease in serum alpha-fetoprotein levels was observed despite the* *lack of effectiveness evaluated by CT scan and angiography. Although minor* *side effects were noted such as a mild degree of *leukocytopenia** * and/or *thrombocytopenia* and hepatic and/or renal dysfunction, they* *were only temporary with a duration of less than 3 or 4 weeks. In 4* *patients with HCC without TAE treatment, however, lethal side effects* *occurred including pancytopenia, hepatic failure and disseminated* *intravascular coagulation, and they died within 2 months after infusion* *chemotherapy. Renal failure was not seen in either group.* **
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* 12/3,AB/56*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05683763 88036929 PMID: 3118094*
* Lupus anticoagulant associated syndrome in benign and malignant systemic* *disease--analysis of ten observations.*
* Duhrsen U; Paar D; Kolbel C; Boekstegers A; Metz-Kurschel U; Wagner R;* *Kirch W; Meusers P; Konig E; Brittinger G*
* Medizinische Klinik und Poliklinik der Universitat (GHS), Essen.* * Klinische Wochenschrift (GERMANY, WEST) Sep 15 *1987*, 65 (18)* * p852-9, ISSN 0023-2173 Journal Code: 2985205R*
* Document type: Journal Article*

* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The clinical and laboratory findings in seven female patients with* *primary autoimmune diseases, one female patient with lymphoplasmacytoid* *(LP) immunocytoma and IgM paraproteinemia, and two male patients with* *multiple myeloma are described. The common denominator in all patients was* *a lupus anticoagulant or a closely related coagulation disorder. Recurrent* *thrombosis was observed in six patients with autoimmune diseases and in two* *patients with malignant monoclonal gammopathies. Other clinical* *manifestations included cerebral disorders (four patients with autoimmune* *disease/two patients with monoclonal gammopathy), repeated obstetric* *complications (6/1), asymptomatic valvular heart disease (6/1), renal* *dysfunction (6/2), hepatic involvement (2/2), and arthropathy (2/0).* *Laboratory investigations revealed a biologic false-positive serological* *test for syphilis in six patients with autoimmune disease and one with* *monoclonal gammopathy, antinuclear antibodies (4/0), antibodies against DNA* *(4/1), and a positive direct Coombs test (3/1) which was accompanied by* *hemolytic anemia in two patients (1/1). Additionally slight* **leukocytopenia* (2/1) and *thrombocytopenia* (6/2) were observed;* *abnormal bleeding was only seen in one patient with severe* **thrombocytopenia* . Other complications characteristic of LP* *immunocytoma or multiple myeloma were missing. The obvious similarities* *between the patients with autoimmune diseases and the patients with* *malignant monoclonal gammopathies suggest analogous pathogenetic* *mechanisms.(ABSTRACT TRUNCATED AT 250 WORDS)*
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* 12/3,AB/57*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05683449 88036615 PMID: 3312721*
* A case report of pulmonary adenocarcinoma responding to (glycolato-0,0')* *diammineplatinum (II), a new platinum complex.*
* Sasaki Y; Ohta T; Tamura T; Eguchi K; Shinkai T; Noguchi M; Saijo N* * Department of Internal Medicine, National Cancer Hospital, Tokyo, Japan.* * Japanese journal of clinical oncology (JAPAN) Sep *1987*, 17 (3)* * p285-90, ISSN 0368-2811 Journal Code: 0313225*
* Document type: Clinical Trial; Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The first patient to respond to [(glycolato-0,0') diammineplatinum (II)]* *(254-S) in a clinical phase I study is reported. The patient was a* *52-year-old man complaining of nausea and weight loss. A chest X-ray* *demonstrated a diffuse infiltrating shadow in the right lung. A* *transbronchoscopic brushing of the right upper lobe and a biopsy specimen* *from the right supraclavicular lymph node revealed adenocarcinoma of the* *lung. He was diagnosed as having primary lung cancer with distant lymph* *node metastasis. 254-S was administered by intravenous drip infusion to a* *dose of 100 mg/m2. Two weeks after the second 254-S treatment, a chest* *X-ray demonstrated a more than 50% reduction in the pulmonary shadow and* *met the WHO criteria for a partial response. *Thrombocytopenia*,* **leukocytopenia* and moderate nausea were observed as adverse effects* *of 254-S but renal toxicity was not found. Pharmacokinetics of free* *platinum in this patient demonstrated biphasic decay with a peak plasma* *concentration of 8.09 micrograms/ml. A disease-oriented phase II study of* *254-S against non-small cell lung cancer should be performed to establish* *the efficacy of this new platinum complex.*
**
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* 12/3,AB/58*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05626401 87305843 PMID: 3476374*
* Effective remission induction in children with recurrent acute myeloid* *leukemia by mAMSA, Ara-C, and VP 16.*
* Berthold F; Creutzig U; Lampert F*
* Hamatologie und Bluttransfusion (GERMANY, WEST) *1987*, 30 p406-9* *, ISSN 0440-0607 Journal Code: 7804332*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Five children treated for acute myeloid leukemia according to the BFM* *protocol AML 83 experienced first bone marrow relapse after 7, 10, 14, 18,* *and 30 months and were retreated for second remission induction. The* *chemotherapy consisted of mAMSA (100 mg/m2 per day i.v., days 1-3), ARA-C* *(100 mg/m2, twice daily, days 1-6), and VP 16 (150 mg/m2 per day, days* *4-6). Four of the children achieved a complete second remission after one* *course of chemotherapy, and the fifth child died of pneumonia during bone* *marrow aplasia. All surviving children received an identical second course* *within 4-5 weeks, followed by maintenance chemotherapy. Remission duration* *was 0, 3, 4, 5, and 5 months. Toxicity was confined to heavy bone marrow* *depression with *thrombocytopenia* (nadir 2-7000, days 7-13) and* **leukocytopenia*

(nadir 0-400, days 8-14). Bleeding episodes could be* *prevented by substitution with platelets. Four patients experienced* *infections (pneumonia, septicemia). We conclude that combination* *chemotherapy using mAMSA, ARA-C, and VP 16 is effective in inducing a* *second remission in patients with early bone marrow relapse. The main side* *effect was considerable bone marrow toxicity.*
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* 12/3,AB/59*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05566161 87245375 PMID: 2885139*
* Electrocardiographic alterations induced by AGEPC in Wistar rats in* *relation to its hypotensive and hematologic effects.* * Tselepis A D; Evangelou A; Tsoukatos D; Demopoulos C A; Kapoulas V M* * Comparative biochemistry and physiology. C, Comparative pharmacology and* *toxicology (ENGLAND) *1987*, 87 (1) p41-6, ISSN 0742-8413* *Journal Code: 8310013*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* AGEPC administration into Wistar rats caused no remarkable* **thrombocytopenia* , slight decrease of the percent count of PMNs in* *whole blood accompanied by anequal *leukocytopenia* and a transient* *increase in hematocrit, due to fluid extraversion. Apart from the dramatic* *fall in blood pressure caused by AGEPC, relatively sinus bradycardia was* *recorded at doses over 6 micrograms/kg b.w. S-T segment elevation, mainly* *evident in II, III and AVF leads, was also recorded within the first* *minutes after AGEPC administration, at doses over 1 microgram/kg b.w. At* *lethal doses, various degrees of A-V block resulting in complete A-V block* *with idioventricular rhythm, or injury pattern resulting in ventricular* *fibrillation or ventricular flutter, were recorded. At sublethal doses no* *arrhythic manifestations were recorded, while S-T segment elevation upward* *inversion became gradually normal.*
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* 12/3,AB/60*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05515179 87194110 PMID: 3032877*
* Multi-modality treatment of primary nonresectable intrahepatic* *cholangiocarcinoma with 131I anti-CEA--a Radiation Therapy Oncology Group* *Study.*
* Stillwagon G B; Order S E; Klein J L; Leichner P K; Leibel S A; Siegelman* *S S; Fishman E K; Ettinger D S; Haulk T; Kopher K; et al* * International journal of radiation oncology, biology, physics (UNITED* *STATES) May *1987*, 13 (5) p687-95, ISSN 0360-3016* *Journal Code: 7603616*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Thirty-seven patients with primary nonresectable intrahepatic* *cholangiocarcinoma (57% with prior treatment and/or metastasis) were* *prospectively treated with external radiation, chemotherapy, and 131I* *labelled anti-CEA. Therapy began in all trials with whole liver irradiation* *(21.0 Gy, 3.0 Gy/Fx, 4 days/week, 10 MV photons) with alternate treatment* *day chemotherapy (Adriamycin, 15 mg + 5-FU, 500 mg). One month after* *external beam therapy, chemotherapy was given (Adriamycin, 15 mg + 5-FU,* *500 mg) followed the next day by the first administration of 131I anti-CEA.* *The treatment schedule used was 20 mCi day 0; 10 mCi day 5 as an* *outpatient. This schedule was derived from tumor dose estimates which* *indicated that 20 mCi (8-10 mCi/mg IgG) was sufficient to achieve tumor* *saturation with a tumor effective half-life of 3 to 5 days, depending upon* *the species of animal from which the antibody was obtained. The median* *tumor dose for the 20 mCi + 10 mCi regimen was 6.2 Gy. Antibody therapy was* *delivered in 2-month cycles using antibody generated in different species* *of animals; rabbit, pig, monkey, and bovine. Toxicity was limited to* *hematologic toxicity and was manifested as *thrombocytopenia* and* **leukocytopenia* (3.2% Grade IV for each according to RTOG toxicity* *criteria). Tumor remission evaluated by CT scan digitized tumor volume* *analysis indicated a 26.6% partial response (PR). Tumor remission by* *physical examination indicated a 33.3% remission rate (25.9% PR and 7.4*% *complete remission (CR]. The median survival for patients who responded was* *15.2 months. The actuarial median survival for the entire group of patients* *(metastases and previous treatment) was 6.5 months. The longest partial* *remission is presently more than 4 years.*
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**
* 12/3,AB/61*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05448295 87126893 PMID: 3028278*
* [Clinical evaluation of MMC-mc-chemoembolization therapy and its* *combination with UFT in hepatocellular carcinoma]*
* Ohmura K; Suzuki M; Takao; Matsuo S K; Ohtsuka Y*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Feb *1987*, 14* * (2) p523-6, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*

* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* A retrospective comparative study was done on the management of hepatoma:* *MMC-mc-chemoembolization therapy (group A; 9 patients) vs. the same therapy* *in combination with UFT as a maintenance therapy (group B; 8 patients). The* *six-month survival rate was 44.4% for group A, and 87.5% for group B.* *Generalized Wilcoxon test for the whole period revealed that the survival* *was favorable for group B as compared with A (P = 0.048). For adverse* *reactions in UFT therapy, no subjective signs occurred, but objective ones* *appeared such as one case of *leukocytopenia*, one of* **thrombocytopenia* and 3 of increased GOT. However, no cessation of UFT* *therapy was necessary in these patients. These findings suggested that* *maintenance therapy with UFT may be favorable in this type of treatment for* *hepatoma.*
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* 12/3,AB/62*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05448293 87126891 PMID: 3813579*
* [Discriminant analysis of bone marrow suppression of methyl*
*6-[3-(2-chloroethyl)-3-nitrosoureido]-6-deoxy-alpha-D-glucopyranoside (MCNU* *)]*
* Saito A; Oride M; Munaka M; Uozumi T*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Feb *1987*, 14* * (2) p511-5, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Twenty-five patients with primary or metastatic brain tumor were treated* *with two administrations of MCNU, 67-125 mg/m2 i.v., at 1-293 day* *intervals. *Thrombocytopenia* of less than 10 X 10(4)/mm8 occurred in 9* *cases (36.0%) and *leukocytopenia* of less than 3 X 10(3)/mm3 in 11* *cases (44.0%). The factors influencing these two kinds of bone marrow* *suppression were investigated using discriminant analysis (SPSS software* *package). The most influential factor for *thrombocytopenia* was the* *dose of MCNU and that for *leukocytopenia* was the interval between the* *two administrations. These results show that patients should be able to* *receive this drug without suffering bone marrow suppression if care is* *taken with regard to their condition with the time interval between doses.* **
**
* 12/3,AB/63*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05424120 87102704 PMID: 3026625*
* Phase I and pharmacokinetic study of trans-N3P3Az2(NHMe)4.* * Mulder N H; Meijers W H; van der Meulen J D; Sleijfer D T; Uges D R; de* *Vries E G; Postmus P E; van de Grampel J C; Willemse P H* * Cancer treatment reports (UNITED STATES) Feb *1987*, 71 (2)* * p155-9, ISSN 0361-5960 Journal Code: 7607107*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* trans-N3P3Az2(NHMe)4, an aziridinyl-substituted cyclophosphazene, was* *tested for its toxicity, pharmacokinetic behavior, and cytostatic activity* *in a phase I study in 30 patients. A total of 66 courses of a single iv* *bolus injection were given in five dose steps. Toxicity consisted of* **leukocytopenia* and *thrombocytopenia*, dose limiting at 70 mg/m2,* *mild anemia, and some nausea. Leukocyte and platelet count nadirs fell* *between 2 and 3 weeks, with recovery at 6 weeks. A tendency for cumulative* **thrombocytopenia* was noticed in three of 13 patients at risk. A* *three-phase plasma elimination model was applicable with t1/2 alpha of 9.9* *minutes, t1/2 beta of 78.5 minutes, and t1/2 gamma of 435.5 minutes; renal* *drug excretion was substantial. Three partial remissions in 21 evaluable* *patients suggest some clinical activity for this drug.* **
**
* 12/3,AB/64*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05396596 87074957 PMID: 2431655*
* [Cisplatin, methotrexate and peplomycin in the treatment of esophageal* *carcinoma]*
* Kagami Y; Sakurai T; Nishio M; Narimatsu N; Saitoh A; Koshiba R; Ikeda H* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Dec *1986*, 13* * (12) p3523-6, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Sixteen patients with advanced or recurrent squamous cell carcinoma of* *the esophagus were treated with cisplatin 80 mg/m2 i.v. on day 1,* *methotrexate 40 mg/m2 i.v. on day 2 and peplomycin 15 mg/day 24 hours* *continuous subcutaneous infusion from day 2 to day 5. Each course was* *repeated every 3 weeks. The overall response rate was 56% (9/16) with no* *complete response. Of 10 patients with no prior therapy, 7 (70%) showed* *partial response. Toxic effects were acceptable with no fatalities, but* *severe nausea and vomiting (56%), transient nephrotoxicity

(44%), anemia* *(44%), *thrombocytopenia* (31%) and *leukocytopenia* (19%)* *occurred. No clinical evidence of pulmonary toxicity was seen. The* *dose-limiting toxic effect of this regimen was myelosuppression.* **
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* 12/3,AB/65*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05369429 87047666 PMID: 3777956*
* [Clinical effects of TA-077 in non-Hodgkin's lymphomas]* * Kobayashi T; Tanaka I; Nishikawa M; Kita K; Matsuoka N; Miwa H; Saitoh M;* *Tsukada T; Shirakawa S*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Oct *1986*, 13* * (11) p3194-7, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Ten patients with non-Hodgkin's lymphomas (NHL), six untreated and four* *with previous chemotherapy, were treated with TA-077, a new derivative of* *nitrosourea. Partial remission was observed in three untreated cases (30%)* *of NHL [Case 1: 71-year-old female with B cell lymphoma/diffuse small cell* *type, Case 2: 79-year-old male with T cell lymphoma/diffuse large cell* *type, and Case 3: 64-year-old female with adult T cell leukemia lymphoma* *(ATLL)]. Remission durations were as follows: Case 1; 33 days, Case 2; 38* *days and Case 3; 14 days. Side effects were transient anorexia (40%),* *nausea & vomiting (30%), liver dysfunction (10%) and delayed hematological* *toxicities (80%). Hematological toxicities consisted of* **leukocytopenia* (80%), *thrombocytopenia* (60%) and anemia (20%).* *Our study suggests that TA-077 is a useful agent as one of the drugs used* *in combination chemotherapy against NHL, since it was effective for* *refractory T cell malignancies such as ATLL.*
**
**
* 12/3,AB/66*
*DIALOG(R)File 155:MEDLINE(R)*
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*05357716 87035930 PMID: 3939496*
* Chemical pathology of diamino acid deficiency: considerations in relation* *to lysinuric protein intolerance.*
* Sidransky H; Verney E*
* Journal of experimental pathology (UNITED STATES) Spring *1985*, 2* * (1) p47-57, ISSN 0730-8485 Journal Code: 8400623* * Contract/Grant No.: AM 27339; AM; NIADDK*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Young rats were force-fed a lysine + arginine-devoid diet or a complete* *diet for 3 days, and selected biochemical and morphologic studies were* *conducted. Rats force-fed the experimental diet in comparison with those* *force-fed the control diet for 3 days showed decreased body weight gain,* *hepatomegaly with periportal fatty liver, pancreatic and splenic atrophy,* *and enhanced 14C-leucine incorporation into hepatic proteins. Differences* *in the experimental animals were observed in the free amino acid levels of* *serum (decreased lysine, arginine, and ornithine) and liver (decreased* *ornithine), in blood chemistries (decreased levels of ammonia N2, uric* *acid, cholesterol, protein, albumin, alkaline phosphatase, LDH and SGOT)* *and in hematologic findings (*leukocytopenia* and* **thrombocytopenia* after a morning feeding). The experimental findings* *in young rats force-fed the lysine + arginine-devoid diet were compared* *with those reported to develop in children with lysinuric protein* *intolerance (LPI), an autosomal recessive defect in diamino acid transport.* *Children with LPI as described by others reveal a number of similarities as* *well as a number of differences in comparison to the findings in the* *experimental animals. The comparison suggests that some of the pathological* *manifestations of LPI may be related to a deficiency of diamino acids but* *others must be due to different alterations in this complex human disease.* **
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* 12/3,AB/67*
*DIALOG(R)File 155:MEDLINE(R)*
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*05320672 86322057 PMID: 3753026*
* [A phase II study of mitoxantrone in refractory and relapsed malignant* *lymphomas. Cooperative Study Group of Mitoxantrone in Malignant Lymphomas]* * Kimura I; Ohnoshi T; Ogawa M; Sampi K; Masaoka T; Yamada K; Ohta K;* *Kitani T; Kawagoe H; Shirakawa S; et al*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Sep *1986*, 13* * (9) p2800-6, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* A phase II clinical trial of mitoxantrone in refractory or relapsed* *malignant lymphomas was conducted by a cooperative study involving 17* *institutions. Of 46 patients entered, 33 were evaluable for responses and* *toxicity. Thirty-one of the 33 had been previously exposed to adriamycin at* *a median dose of 220 mg/m2 (range 21-489 mg/m2), and two additional* *patients had each been given THP-adriamycin

at a dose of 80 mg/m2 or 4'-epi* *adriamycin at a dose of 69 mg/m2. Mitoxantrone was administered in 3* *different schedules: 8-12 mg/m2, every 3-4 weeks in 23 patients; 4-6 mg/m2,* *weekly, in 3 patients; and 2-4 mg/m2, for 5 days, in 7 patients.* *Summarizing the responses obtained in the 3 schedules, there were 2 partial* *responders among 5 with Hodgkin's disease, while there were 8 complete* *responders and 4 partial responders among 28 with non-Hodgkin's lymphoma.* *The overall response rate for all the evaluable patients was 42% with a* *complete response rate of 24%. The median response duration was 7+ weeks* *(range 4-27+ weeks) for complete responders and 7 weeks (range 4-46+ weeks)* *for partial responders. The major toxicity was myelosuppression:* **leukocytopenia* less than 3,000/microliter occurred in 79% of* *patients, and *thrombocytopenia* less than 75,000/microliter in 35%.* *Other toxic effects were minimal, mild nausea and/or vomiting occurred in* *39%, and diarrhea in 3%. Possible drug-related liver and renal dysfunctions* *were observed in 19% and 10%, respectively. The favorable response to* *mitoxantrone in patients with prior anthracycline antibiotic therapy* *suggests that the drug is not fully cross-resistant with anthracycline* *antibiotics, and that this drug is of value in combination with other drugs* *as a salvage therapy for patients with refractory or relapsed malignant* *lymphomas.* **

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*05281028 86282293 PMID: 3735704*

* Phase II study of mitoxantrone in patients with non-small cell lung* *cancer.*

* Suga J; Saijo N; Shinkai T; Eguchi K; Sasaki Y; Sakurai M; Sano T; Tamura* *T; Hoshi A*

* Japanese journal of clinical oncology (JAPAN) Jun *1986*, 16 (2)* * p147-51, ISSN 0368-2811 Journal Code: 0313225*

* Document type: Journal Article*

* Languages: ENGLISH*

* Main Citation Owner: NLM*

* Record type: Completed*

* A phase II study of mitoxantrone was performed in 24 patients with* *non-small cell lung cancer (NSCLC). Mitoxantrone was administered by* *intravenous drip infusion of 12 mg/m2 every three weeks. There were no* *responders among the 21 evaluable patients including five patients without* *prior therapy. The major hematological toxic effect was* **leukocytopenia*. *Thrombocytopenia* and decrease in hemoglobin* *were slight. A change in the electrocardiogram was observed in one patient* *and one patient experienced cardiogenic shock. Mitoxantrone is not* *acceptable for the treatment of NSCLC because of its low antitumor* *activity, and careful observation is needed for administration of this* *agent to patients with pre-existing risk factors, such as prior* *anthracycline exposure, mediastinal radiation or underlying cardiovascular* *disease.*

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* 12/3,AB/69*

*DIALOG(R)File 155:MEDLINE(R)*

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*05266698 86267863 PMID: 3089174*

* [Intraarterial bolus infusion followed by rapid removal of anticancer* *agents with hemocarboperfusion under local hyperthermia in advanced hepatic* *cancer]*

* Agishi T; Nakazawa H; Teraoka S; Fuchinoue S; Okumura T; Ota K; Akimoto S* *; Hamano K*

* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Apr *1986*, 13* * (4 Pt 2) p1611-7, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*

* Languages: JAPANESE*

* Main Citation Owner: NLM*

* Record type: Completed*

* Reported herein is a new multidisciplinary treatment modality for* *unresectable hepatic cancer in which local hyperthermia and intraarterial* *infusion of bolus anticancer agent are simultaneously undertaken while* *anticancer agent leaking from the hepatic bed into the general circulation* *is rapidly removed by charcoal hemoperfusion. Local hyperthermia induced by* *exposure to 13.56-MHz radiofrequency waves was conducted between one and* *one and a half hours once or twice a week. During the hyperthermia* *treatment, a bolus of either 1 mg/kg Mitomycin C or 2 mg/kg Adriamycin was* *injected into the hepatic artery via a Vascular Access Port, the catheter* *portion of which had been surgically inserted into the hepatic artery and* *the reservoir of which had been implanted subcutaneously. In general, a* *regular dose of 6 mg of Mitomycin C was injected into the Vascular Access* *Port during the following hyperthermia procedures. In seven of nine* *patients (78%) treated with this method, a marked reduction in tumor size* *of more than 50% was observed on computed tomograms. A light to moderate* *degree of side effects such as *leukocytopenia*, *thrombocytopenia** *, liver dysfunction or hair loss were noticed after the bolus infusion, but* *were not so serious as to threaten the patients' lives.* **

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* 12/3,AB/70*

*DIALOG(R)File 155:MEDLINE(R)*

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*05239823 86240915 PMID: 3013099*

* [Combination chemotherapy with cis-platinum, adriamycin and mitomycin C* *(PAM) in the treatment of non-small cell carcinoma of the lung]* * Nakano H; Kurihara M; Saito R; Takise A; Tsuchiya S; Minato K; Takehara K* *; Saruya T; Kuwabara H; Fueki R; et al*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jun *1986*, 13* * (6) p2123-7, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Twenty-three patients with inoperable non-small cell lung cancer were* *treated with a combination chemotherapy of CDDP 100 mg/m2, ADM 30 mg/m2 and* *MMC 8 mg/m2 (PAM). Ten cases were adenocarcinoma, 9 cases were squamous* *cell carcinoma and 4 cases were large cell carcinoma. In 21 evaluable* *cases, partial response was obtained in 47.6%. (The response rates were* *40.0% in patients with adenocarcinoma, 50.0% in those with squamous cell* *carcinoma and 66.7% in those with large cell carcinoma.)* **Leukocytopenia* of less than 4,000/mm3 occurred in 100% of cases,* **thrombocytopenia* of less than 100,000/mm3 occurred in 81.0%, and* *anemia(fall in hemoglobin over 2.0 g/dl) occurred in 66.7%. A transient* *elevation of Cr (over 1.5 mg/dl) and/or BUN (over 30 mg/dl) was observed in* *23.8%. Nausea and vomiting occurred in almost all patients. No death* *occurred due to toxicity of PAM. These results demonstrate that PAM is an* *effective combination chemotherapy in patients with non-small cell* *carcinoma of the lung.*
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* 12/3,AB/71*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05216809 86217837 PMID: 3708608*
* High-dose teniposide for refractory malignancies: a phase I study.* * de Vries E G; Mulder N H; Postmus P E; Vriesendorp R; Willemse P H;* *Sleijfer D T*
* Cancer treatment reports (UNITED STATES) May *1986*, 70 (5)* * p595-8, ISSN 0361-5960 Journal Code: 7607107*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* To evaluate the dose-limiting toxicity of teniposide (VM-26), a phase I* *study was conducted. VM-26, a semisynthetic podophyllotoxin derivative, was* *administered on 3 consecutive days. The initial total dose per course was* *0.3 g/m2, with dose escalation to 0.6 and 1 g/m2. The most prominent side* *effects observed were severe skin rash in all three patients in the highest* *dose group and a dose-dependent degree of *leukocytopenia* and* **thrombocytopenia* . In the highest dose group the leukocyte count in* *all courses was less than 1 X 10(9) cells/L and in three of five courses* *the platelet count was less than 25 X 10(9) cells/L. Of the 13 evaluable* *patients, five had partial remission, one had minor response, and four had* *stable disease. Further study should be centered on phase II studies in* *selected tumor groups at a VM-26 dose of 0.6 g/m2.*
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* 12/3,AB/72*
*DIALOG(R)File 155:MEDLINE(R)*
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*05150986 86151739 PMID: 3754064*
* A preliminary analysis of combination therapy with vincristine,* *adriamycin, and prednimustine (VAP) in advanced breast cancer: a phase II* *study.*
* Lehnert M; Biffl G; Wascher H; Jordis-Lohausen K; Wahlby S* * Seminars in oncology (UNITED STATES) Mar *1986*, 13 (1 Suppl 1)* * p32-4, ISSN 0093-7754 Journal Code: 0420432*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Between March 1984 and May 1985, 29 patients with metastatic breast* *cancer and high-risk prognostic factors were treated with vincristine, 1.4* *mg/m2 IV on day 1, Adriamycin, 40 mg/m2 IV on day 1, and prednimustine, 100* *mg/m2 PO on days 3 to 7. Courses were repeated every 3 weeks. At the* *present time, 26 patients are evaluable for tumor response; 29 are* *evaluable for toxicity. Fourteen of 26 patients (53.8%) achieved a partial* *response lasting 2 to 9 months (median 5.5+). A complete response was not* *recorded. Ten of 26 patients (38.5%) had stable disease; two patients* *(7.7%) showed a primary tumor progression. Most common side effects were* *nausea, vomiting, and alopecia, all generally mild to moderate. Fourteen of* *29 patients developed *leukocytopenia*, mainly of WHO grade 1;* **thrombocytopenia* was registered in one patient only and a fall of* *hemoglobin in three patients only. In 15 patients, no hematologic toxicity* *occurred. These preliminary data suggest good antitumor activity and* *acceptable toxicity for vincristine-Adriamycin-prednimustine in patients* *with metastatic breast cancer.*
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* 12/3,AB/73*
*DIALOG(R)File 155:MEDLINE(R)*
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*05126168 86126777 PMID: 4091143*
* [A case of cavernous hemangioma of the testis]*

* Ogawa O; Yoshimura N; Nishimura K; Nakagawa T; Nagata Y* * Hinyokika kiyo. Acta urologica Japonica (JAPAN) Nov *1985*, 31* * (11) p2060-4, ISSN 0018-1994 Journal Code: 0421145* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Non-germinal cell tumor of the testis is a rare disease, and vascular* *tumor of the testis is a still rarer disease. Herein, a case of cavernous* *hemangioma of the testis is reported. A 75-year-old man consulted our* *department with the complaint of a painless left intrascrotal tumor.* *Laboratory findings revealed slight *leukocytopenia* and* **thrombocytopenia* of unknown origin. In chest X-ray, a diffuse* *reticular shadow was shown and it was considered due to pulmonary fibrosis,* *but, alpha-fetoprotein and CEA were normal. Left radical orchiectomy was* *performed under spinal anesthesia. The tumor existed under the tunica* *albuginea, and the cutting surface of the tumor was brown and irregular.* *There were hemorrhagic portions in some places. The left epididymis and the* *left spermatic cord were normal. Histologically, the tumor was diagnosed as* *cavernous hemangioma. The vascular tumor of the testis is a very rare* *disease, and only 17 cases have been reported including this case. This* *case was the 7th case of cavernous hemangioma of the testis, and the first* *case in Japan. This patient died of respiratory failure due to pulmonary* *fibrosis and pneumonia. In the autopsy, there was no abnormal finding that* *was considered to be related to the cavernous hemangioma of the testis.* **
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* 12/3,AB/74*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05099703 86100140 PMID: 4083212*
* [Histopathologic evaluation of anti-tumor activity of alpha-interferon* *for renal cell carcinoma, especially in autoptic cases]* * Yamauchi T; Kawamura J; Yoshida O; Fukuyama T; Ogura K; Nakagawa K* * Hinyokika kiyo. Acta urologica Japonica (JAPAN) Sep *1985*, 31* * (9) p1539-52, ISSN 0018-1994 Journal Code: 0421145* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* The anti-tumor activity of alpha-interferon (gamma-IFN-alpha A) was* *assessed histopathologically in 14 patients with metastasized renal cell* *carcinoma. Ten of the patients had undergone radical nephrectomy, two* *patients embolization alone, one patient no prior treatment and one patient* *nephrectomy in IFN therapy. IFN was given daily intramuscularly starting at* *the dose of 3 X 10(6) U and increased every 3 days to the maximum of 5 X* *10(7) U. This treatment could be tolerated. The clinical response was* *evaluated according to the criteria of Koyama and Saitou. Two of the* *patients showed partial response, one patient minor response, five patients* *no change and six patients progressive disease. The clinical responders* *also had histopathologically detected improvement. Renal cell carcinoma of* *a higher grade (sarcomatoid type) or lower grade (grade II greater than or* *equal to), was seen frequently, and the papillary or tubular type was* *resistant to IFN. The clear cell type and grade III tumor was more* *responsive to IFN. Histopathologically, no lymphocyte infiltration into the* *cancer cell focus was seen and the immunologic reaction was not considered* *to be affected by IFN, because of the myelosuppression due to the IFN* *therapy and because more responders used the steroid hormone like* *predonizolone to prevent side effects. Fever, anorexia and general malaise* *were observed in all cases. Myelosuppression like *leukocytopenia** * and/or *thrombocytopenia* was also observed but easily improved after* *cessation of IFN medication or decrease of IFN dose. Liver dysfunction was* *observed but spontaneous recovery without discontinuation of IFN therapy or* *decrease of IFN dose was seen in two cases. The disturbance of the central* *nervous system similar to the occurrence of abnormal EEG waves or* *psychosis, was a dose-limiting factor. Further studies especially to* *develop an appropriate method of administration and the combination with* *other anti-cancer agents must be studied.*
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* 12/3,AB/75*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05075654 86075994 PMID: 2934023*
* [Intra-arterial infusion chemotherapy with anticancer agents for advanced* *breast cancer--effect and toxicity of mitomycin C and adriamycin]* * Toda K; Asaishi K; Okazaki A; Okazaki Y; Okazaki M; Ebata T; Totsuka M;* *Hayasaka H; Sato N; Narimatsu E*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Dec *1985*, 12* * (12) p2298-304, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* In 23 cases of primary advanced breast cancer, intra-arterial infusion* *chemotherapy of Adriamycin (ADR) and Mitomycin C (MMC), which were injected* *jointly or individually, was performed and its effects

and side effects* *were studied. As for the clinical effects, the response rate (CR + PR) was* *73.9% (17/23 cases) and the histological response rate (greater than grade* *IIb) was 82.6% (19/23 cases). ADR alone (100-150 mg) and MMC (28 mg) + ADR* *(42 mg) combined regimens were especially superior in both their clinical* *and histological effects. In metastatic lymph nodes, the histological* *response rate was 78.9% (15/19 cases). As for the side effects, in the* *cases treated with MMC, bone marrow suppression such as* **leukocytopenia* and *thrombocytopenia* was remarkable and took a* *long time to recover. The above results suggested that the most effective* *regimen for primary advanced breast cancer using intra-arterial infusion* *chemotherapy is ADR alone, in single doses of 50 mg up to a total dose of* *150-200 mg. Histological examination of the effective cases revealed that* *the central region of the tumor was more markedly recrotic than the* *periphery. It was suggested that the grade of the effects on tumor tissues* *is related to the mechanism of anticancer agents.*
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* 12/3,AB/76*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*05027422 86027623 PMID: 4052926*
* Clinical results of leukocyte interferon-induced tumor regression in* *resistant human metastatic cancer resistant to chemotherapy and/or* *radiotherapy-pulse therapy schedule.*
* Medenica R; Slack N*
* Cancer drug delivery (UNITED STATES) Winter *1985*, 2 (1) p53-76* *, ISSN 0732-9482 Journal Code: 8409965*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The efficacy of Human 6 IFN (HLIFN) given in a pulse fashion was* *determined in a phase II study. Ninety-one cancer patients were evaluated* *(9 myeloma, 12 breast, 14 prostate, 9 melanoma, 4 renal, 6 astrocytoma, 7* *ovarian, 9 large bowel, 7 gastric, 14 head and neck). They all had advanced* *progressive cancer that was resistant to chemotherapy and/or radiotherapy.* *Patients were treated by intramuscular injection of 6 X 10(2) I.U./m2 for* *three consecutive days every four weeks. 84 patients were evaluable.* *Complete clinical response was obtained in 23 patients (4 myeloma, 2* *breast, 5 prostate, 1 melanoma, 1 renal, 2 astrocytoma, 2 ovarian, 2 large* *bowel, 1 gastric, 3 head and neck). Partial responses were observed in 35* *patients (3 myeloma, 7 breast, 6 prostate, 4 melanoma, 1 renal, 2* *astrocytoma, 3 ovarian, 4 head and neck). Objective responses were related* *(P less than 0.01) to serum IFN level, with complete and partial responses* *(P less than 0.01) more commonly seen in those patients whose serum IFN* *levels at two hours were in the range of 1000 to 1650 I.U./ml. Side effects* *resulting from pulse IFN were acceptable for this group of patients and* *consisted of fever, transient chills, malaise and asthenia, and transient* **thrombocytopenia* and *leukocytopenia* . The extent of fever was* *directly related (P less than 0.01) to response, and was most elevated in* *patients who achieved objective responses. IFN administered in a pulse* *fashion appears to be more effective than daily IFN and merits further* *evaluation.*
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* 12/3,AB/77*
*DIALOG(R)File 155:MEDLINE(R)*
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*04958430 85265314 PMID: 4021119*
* Preliminary phase II study of adriamycin (ADM) in patients with non-small* *cell lung cancer (NSCLC).*
* Fujita J; Saijo N; Eguchi K; Shinkai T; Tominaga K; Sasaki Y; Sakurai M;* *Futami H; Ishihara J; Takahashi H; et al*
* Japanese journal of clinical oncology (JAPAN) Jun *1985*, 15 (2)* * p365-8, ISSN 0368-2811 Journal Code: 0313225*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* A phase II study of adriamycin (ADM) (60 mg/m2) was performed in 22* *patients with non-small cell lung carcinoma (NSCLC). There were no* *responders in the 19 evaluable patients (16 with adenocarcinoma, two with* *squamous cell carcinoma and one with large cell carcinoma). The major side* *effects were alopecia (89%), *leukocytopenia* (73%),* **thrombocytopenia* (58%) and upper gastrointestinal symptoms. Although* *ADM at 60 mg/m2 did not appear to have sufficient antitumor activity* *against NSCLC in this study, it is necessary to evaluate further the* *efficacy of ADM against NSCLC with another treatment schedule.* **
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* 12/3,AB/78*
*DIALOG(R)File 155:MEDLINE(R)*
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*04948438 85255316 PMID: 3893780*
* Phase I study of the cisplatin analogue 1,1-diamminomethylcyclohexane* *sulfatoplatinum (TNO-6) (NSC 311056).*
* Sorensen J B; Groth S; Hansen S W; Nissen M H; Rorth M; Hansen H H* * Cancer chemotherapy and pharmacology (GERMANY, WEST) *1985*, 15* * (2)

p97-100, ISSN 0344-5704 Journal Code: 7806519* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* The cisplatin derivative TNO-6 was evaluated for clinical toxicity in a* *phase I trial. TNO-6 was given daily for 5 days every 3 weeks as a 30-min* *IV infusion without hydration. In all, 39 patients with advanced cancer* *were treated at doses of 2.5-9.0 mg/m2. No dose-limiting nephrotoxicity* *occurred, but evidence of mild, reversible tubular damage was found.* *Dose-limiting toxicity was hematologic with both thrombopenia and* **leukocytopenia* , which with high dose levels reached WHO grade 4.* *Hematologic toxicity was most pronounced for pretreated patients. No* *antitumor activity was seen. The recommended dose for phase II trials will* *be 9.0 mg/m2 for previously untreated and 8.0 mg/m2 for pretreated* *patients.*
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* 12/3,AB/79*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04917593 85224311 PMID: 3859252*
* [Combination chemotherapy with cyclophosphamide, adriamycin, cisplatin,* *nimustine(ACNU), and methotrexate (EACAM) in advanced adenocarcinoma of the* *lung]*
* Nakanishi F; Sugiishi M; Ogasawara T; Sugiura I; Kinoshita T; Ito Y;* *Hoshino A*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jun *1985*, 12* * (6) p1339-44, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Twenty-two patients with advanced adenocarcinoma of the lung were treated* *with the combination chemotherapy "EACAM" consisting of cyclophosphamide* *(333mg/m2 X 1), adriamycin (27mg/m2 X 1), cisplatin (25mg X 5), nimustine* *(33mg/m2 X 1), and methotrexate (27mg/m2 X 3). This regimen was repeated* *once every 4 or 5 weeks. One complete response (CR) and 8 partial responses* *(PR) were obtained in 21 evaluable patients and the response rate was* *42.9%. It has not been possible to calculate the median survival time for* *all of the evaluable cases, since 13 of them are still alive up to the* *present time. The side effects observes were as follows: nausea and* *vomiting (81.8%), alopecia (81.8%), stomatitis (22.7%),* **leukocytopenia* less than 2,000/mm3 (45.5%), and* **thrombocytopenia* less than 5 X 10(4)/mm3 (18.2%). Apart from strong* *myelosuppression, no severe infection or bleeding tendency was noticed. A* *mild elevation of serum createnine was observed in one patient, and no* *patients developed renal insufficiency. The combination chemotherapy* *"EACAM" is therefore considered to be a very effective and tolerable* *treatment for adenocarcinoma of the lung.*
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* 12/3,AB/80*
*DIALOG(R)File 155:MEDLINE(R)*
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*04917558 85224276 PMID: 3859248*
* [Phase II study of methyl 6-[3-(2-chloroethyl)-3-nitrosoureido]-6-deoxy-a* *lpha-D-glucopyranoside (MCNU).]*
* Tanaka I; Kobayashi T; Shirakawa S; Ikeda Y; Kobayashi M; Yamagata K;* *Ohta K; Ohno R; Yamada H; Yamada K; et al*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Mar *1985*, 12* * (3 Pt 1) p493-8, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Sixty-seven patients with hematological malignancies and 4 with cancers* *were evaluated in this study. Standard administration of MCNU was* *instituted intravenously using 50-100 mg/m2 every 2 or 4 weeks, whereas* *some cases were treated with a higher dose therapy. Of 10 patients with* *chronic myelogenous leukemia, 7 achieved complete remission (CR), and 1* *achieved partial remission (PR). A good response was also obtained in 9 of* *10 patients with polycythemia vera and in all 4 patients with essential* *thrombocythemia. MCNU was less effective in malignant lymphoma (ML) and* *multiple myeloma (MM) than in myeloproliferative disorders. Two of 15* *patients with ML and one of 21 patients with MM achieved CR, and two with* *ML and three MM achieved PR. Three patients with lung cancer and 1 with* *gastric cancer showed no response to MCNU. Delayed anemia,* **leukocytopenia* and *thrombocytopenia* were observed in 38.7% of* *patients, and these were regarded as major side effects of MCNU. Nausea,* *vomiting, anorexia and elevated transaminase were also found in about 24*% *of patients, but only transiently. Our study indicates that MCNU is useful* *for chemotherapy of hematological malignancies, especially of* *myeloproliferative disorders. Therefore, further studies on combination* *chemotherapy with MCNU should be developed.*
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*04814718 85120963 PMID: 2578770*
* [Combined chemotherapy for head and neck cancer using cisplatin,* *methotrexate and continuous subcutaneous infusion of peplomycin]* * Kagami Y; Nishio M; Saitoh A; Doi Y; Asano K; Sakurai T; Murakami Y;* *Narimatsu N*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Feb *1985*, 12* * (2) p337-42, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Twenty-one patients with advanced or recurrent squamous cell carcinoma of* *the head and neck were treated with cisplatin, methotrexate and continuous* *subcutaneous infusion of peplomycin. The overall response rate was 62*% *(13/21) with 19% (4/21) complete response. The median duration of partial* *response was 2 months, while that of complete response was 3 months. Toxic* *effects were acceptable with no fatalities, but nephrotoxicity (33%),* **leukocytopenia* (24%), *thrombocytopenia* (29%) and severe nausea* *and vomiting (76%) occurred. Pulmonary toxicity due to continuous* *subcutaneous infusion of peplomycin (15 mg/day, 4 days) was not seen.* **
**
* 12/3,AB/82*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04802368 85108599 PMID: 6240546*
* Phase II study of oral administration of 5'-deoxy-5-fluorouridine* *(5'-DFUR) for solid tumors.*
* Shimizu E; Saijo N; Eguchi K; Shinkai T; Tominaga K; Sasaki Y; Fujita J;* *Nomori H; Hoshi A*
* Japanese journal of clinical oncology (JAPAN) Dec *1984*, 14 (4)* * p679-83, ISSN 0368-2811 Journal Code: 0313225*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* A phase II trial of 5'-deoxy-5-fluorouridine (5'-DFUR), a new fluorinated* *pyrimidine analog which has been demonstrated to have potential superiority* *over 5-FU and tegafur for chemotherapy of murine tumors, was performed in* *patients with advanced non-small cell carcinoma of the lung and metastatic* *pulmonary tumors. 5'-DFUR at a dose of 800 mg/m2 was given per os every day* *for more than four weeks. None of 15 evaluable patients with non-small cell* *carcinoma of the lung and 15 evaluable patients with metastatic pulmonary* *tumors showed a complete or partial response. Toxic effects of 5'-DFUR* *included anorexia (29%), diarrhea (26%), nausea (23%), vomiting (10%),* **leukocytopenia* (10%), general fatigue (10%), liver disorder (6%) and* **thrombocytopenia* (6%).*
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* 12/3,AB/83*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04765118 85071162 PMID: 6095762*
* [Cisplatin, adriamycin and VP-16 (CAV) in the treatment of small cell* *carcinoma of the lung]*
* Yokoyama A; Kinameri K; Kurita Y*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Dec *1984*, 11* * (12 Pt 1) p2573-8, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Sixteen patients with small cell carcinoma of the lung were treated with* *a combination of cisplatin (25 mg X 5 or 80 mg/m2 X 1), adriamycin (30* *mg/m2 X 1) and VP-16 (200 mg (p.o) X 5) every 3-4 weeks. Nine of these* *patients had received prior therapy. In 12 evaluable patients, there were 9* *partial responses and 1 complete response, giving a total response rate of* *83.3% (10/12). 6 of 10 responders received radiation therapy after* *induction chemotherapy, and 4 patients achieved complete response. The* *median survival time of responders was 52 weeks. The major toxic effects* *included nausea and vomiting (81%), *leukocytopenia* less than 2,000* *(75%), and *thrombocytopenia* less than 10 X 10(4) (44%). Renal* *toxicity was mild and none of these patients developed renal insufficiency.* *These results demonstrate that CAV is an effective regimen for remission* *induction chemotherapy in patients with small cell carcinoma of the lung.* **
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* 12/3,AB/84*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04765108 85071152 PMID: 6508315*
* [Phase II study of KW 2083 [7-N-(p-hydroxyphenyl)-mitomycin C] in* *patients with various cancers]*
* Nishi I; Yokoyama T; Nakao I; Harashima S; Ohashi Y; Kanko T; Saito T* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Dec *1984*, 11* * (12 Pt 1) p2513-9, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* A phase II study of KW 2083

[7-N-(p-Hydroxyphenyl)-Mitomycin C] was* *carried out in 14 cases of stomach cancer, 5 of lung cancer, 5 of colon* *cancer and 5 other types of cancer. KW 2083 was intravenously injected at a* *dose of 40 mg/body weekly in 26 cases. Among 23 evaluable cases, partial* *response was obtained in 6 cases (26%). The PR cases were 4 of stomach* *cancer and 2 of lung cancer, the former being all undifferentiated* *adenocarcinoma. Regarding hematologic toxicities, *thrombocytopenia** * was the most principal toxicity and an important weak point of KW 2083.* **Thrombocytopenia* (less than 75,000/mm3) was observed in 13 cases* *(50%). Recovery took about 4 weeks, but by that time 3 cases had still not* *recovered to 75,000/mm3. *leukocytopenia* (less than 3,000/mm3) was* *observed in 17 cases (65%). Concerning gastrointestinal symptoms, anorexia* *occurred in 11 cases (42%), nausea and vomiting in 11 cases (42%), diarrhea* *in 1 case and stomatitis in 1 case. T1/2 (beta-phase) of KW 2083 was half* *that of Mitomycin C.*
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* 12/3,AB/85*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04662283 84305918 PMID: 6591857*
* [Effects of 4'-Epi-adriamycin, THP-adriamycin and mitoxantrone on* *patients with advanced and recurrent breast cancer]*
* Tominaga T; Kitamura M; Hayashi K; Takahashi I; Kosaki G* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Aug *1984*, 11* * (8) p1669-74, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* The therapeutic effects of 4'-Epi-Adriamycin (Epi-ADR), THP-Adriamycin* *(THP-ADR) and Mitoxantrone on 30 patients with advanced and recurrent* *breast cancer were analyzed. Responders for Epi-ADR, THP-ADR and* *Mitoxantrone were 5/18, 3/8 and 2/8 respectively. *Leukocytopenia* less* *than 3000 was observed in 7/12 for Epi-ADR, 8/8 for THP-ADR and 7/8 for* *Mitoxantrone. *Thrombocytopenia* was found in 2 cases treated with* *Epi-ADR. Gastrointestinal disorders were observed in patients treated with* *Epi-ADR extensively with THP-ADR moderately and with Mitoxantrone slightly.* *Marked alopecia was remarkably seen in.the patients treated with Epi-ADR,* *but it was only slight in those treated with THP-ADR and Mitoxantrone. No* *cardiotoxicity was recorded in any of the patients.*
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* 12/3,AB/86*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04510078 84152836 PMID: 6538404*
* [Analysis of side effects of a combination chemotherapy of cisplatin and* *adriamycin in gynecological malignancies: comparison between intravenous* *and intraarterial administration]*
* Kawagoe K; Tsunoda H; Iijima S; Yokota H; Shigemitsu S* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Mar *1984*, 11* * (3) p452-7, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* In 23 cases of gynecological malignancies, comparative analysis of the* *side effects of a combination chemotherapy of cisplatinum (CDDP) and* *adriamycin (ADM) was performed in terms of administration routes:* *intravenous and intraarterial. 50 mg/m2 of CDDP and 50 mg/m2 of ADM were* *administered intravenously once for three weeks. 12.5 mg of CDDP and 10 mg* *of ADM per one catheter were infused intraarterially once or twice a week.* *More than severe *leukocytopenia* was observed in all cases of systemic* *administration, while in 25% of intraarterial infusion. In 90% of* *intravenous administration and in about a half of intraarterial cases,* **thrombocytopenia* was noted. Myelosuppression was severest at 10 the* *to 12th day after administration. The value of creatinine clearance (C-Cr)* *was within normal limits in 10% of cases of intravenous and in nearly 50*% *of cases of intraarterial administration. No mortal cases due to* *myelosuppression and no renal failure ware observed. Most cases of* *intravenous administration were suffered from severe vomiting, while only* *in half cases of intraarterial chemotherapy milder emesis appeared.* *Antiemetic drugs should be administered at least for one week after* *systemic chemotherapy, and also intraarterial chemotherapy, if necessary.* **
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* 12/3,AB/87*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04493298 84135954 PMID: 6583205*
* 4'-Epi-Doxorubicin -- a clinical phase-II trial in solid tumors.* * Schutte J; Niederle N; Grunenberg B; Krischke W; Seeber S; Schmidt C G* * Journal of cancer research and clinical oncology (GERMANY, WEST)* **1984*, 107 (1) p38-41, ISSN 0171-5216 Journal Code: 7902060* * Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*

* Record type: Completed*
* 4'-Epi-doxorubicin is a new anthracycline analog with reduced cardiac* *toxicity in animal studies. A phase-II study was performed in 17 patients* *predominantly with non-small-cell lung cancer. All suffered from recurrent* *or advanced tumors and 7 of 16 evaluable patients had been pretreated with* *an alternative chemotherapy. 4'-Epi-doxorubicin was applied at a dose of 75* *mg/m2 every 3-4 weeks. The median total dose was 280 mg (range: 130-250* *mg). Only one patient with epidermoid lung cancer (overall response rate:* *6%) showed a minor response and stable disease was observed in six other* *patients with bronchogenic carcinoma. Myelosuppression was rare and* *moderate: *leukocytopenia* of less than 2,000/mm3 occurred in 25% of* *patients and *thrombocytopenia* of less than 100,000/mm3 in 8% of* *patients. The frequency of alopecia and gastrointestinal side effects was* *88% and 80%, respectively. Persistent electrocardiographic alterations were* *recorded in 2 of 14 (14%) patients. One of four patients revealed a marked* *reduction of left ventricular ejection fraction in radionuclide* *cardiography. It is concluded that 4'-epi-doxorubicin is not superior to* *adriamycin in this low-prospect treatment area, but studies with increased* *doses appear necessary in adriamycin-sensitive tumors because of recent* *reports from phase-III trials showing reduced cardiac and gastrointestinal* *toxicity with 4'-epi-doxorubicin in comparison with adriamycin.* **
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* 12/3,AB/88*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04448091 84090458 PMID: 6197540*
* New preoperative chemotherapy for bladder cancer using combination* *hemodialysis and direct hemoperfusion: preliminary report.* * Kamidono S; Fujii A; Hamami G; Nakano Y; Umezu K; Oda Y; Ishigami J* * Journal of urology (UNITED STATES) Jan *1984*, 131 (1) p36-40,* *ISSN 0022-5347 Journal Code: 0376374*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Preoperative chemotherapy and subsequent cystectomy were performed on 11* *patients with locally invasive bladder cancer. Three chemotherapy regimens* *were tested: 1) 2 to 3 mg. per kg. doxorubicin in 5 patients, 2) 1 mg. per* *kg. mitomycin C in 3 and 3) 0.6 mg. per kg. mitomycin C with 70 mg.* *systemic bleomycin in 3. Doxorubicin and mitomycin C were infused once* *preoperatively into the hypogastric arteries or the aortic bifurcation,* *with simultaneous hemodialysis and direct hemoperfusion to remove as much* *extra-regional infusate as possible and, thus, reduce the systemic toxicity* *of the drug. Objective responses were obtained in 4 of 7 patients with* *measurable tumor (57 per cent). Downstaging was obtained in 7 of 11* *patients (64 per cent). All patients given doxorubicin had* **leukocytopenia* (500 to 1,900 per mm.3) and moderate patchy alopecia,* *and 1 patient given mitomycin C and bleomycin had *thrombocytopenia** *(44,000 per mm.3). However, these side effects were observed comparatively* *less in the patients given mitomycin C only.*
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* 12/3,AB/89*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04380905 84022615 PMID: 6414382*
* [Combination of intra-arterial administration of anticancer agent and* *hemocarboperfusion in treatment of advanced cancer]*
* Yamagata J; Agishi T; Ota K; Shida K; Shibayama K; Yamanaka E; Hata H;* *Nagata T; Ishigami J; Kamidono S; et al*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Oct *1983*, 10* * (10) p2139-44, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Nineteen patients with malignant tumors were treated with a combination* *of bolus administration of mitomycin C with direct hemoperfusion over* *charcoal, and 15 patients were valuable. Mitomycin C of 1 mg/kg was* *administered via a catheter placed into the regional artery. Seven out of* *14 patients with genitourinary cancers: 4 out of 9 patients with urinary* *bladder, 2 of 4 patients with renal and one prostate responded to the* *therapy. There were 4 responders out of 8 in the one-shot administration* *group, on the other hand, 7 cases receiving continuous infusion of 60 to* *120 minutes responded. In both the one-shot group and the continuous group* *nausea and vomiting were observed in 21% and 11% respectively. Three* *patients receiving continuous administration of mitomycin C had local* *ulcerations. Myelosuppressions such as *leukocytopenia* and* **thrombocytopenia* were observed in 37% of the both groups.* **
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* 12/3,AB/90*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04151656 83281720 PMID: 6882001*
* [Phase II study of KW2083 [7-N-(p-hydroxyphenyl)-mitomycin C] in patients* *with carcinoma of the lung and metastatic pulmonary tumor]* * Shinkai T; Saijo N; Tominaga K; Eguchi K; Shimizu E;

Shibuya M;* *Shimabukuro Z*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Mar *1983*, 10* * (3) p834-9, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* A phase II study of KW2083 [7-N-(p-Hydroxyphenyl)-Mitomycin C], a* *derivative of Mitomycin C, was carried out in 20 patients with carcinoma of* *the lung and in 19 patients with metastatic pulmonary tumor. KW2083 was* *administered by single intravenous injection at a dose of 20-30 mg/m2* *weekly or a single 70 mg/m2 dose. Patients treated with a dose of 20-30* *mg/m2 should be given at least 3 doses for eligibility. Of 17 evaluable* *patients with carcinoma of the lung (11 adenocarcinomas, 3 squamous cell* *carcinomas, 2 small cell carcinomas and 1 large cell carcinoma), two* *patients with adenocarcinoma showed a partial response (11.8%). Two* *patients who achieved PR had adenocarcinoma without prior therapy received* *KW2083 at a single dose of 70 mg/m2 Objective response rates were 18.2% for* *11 patients with adenocarcinoma and 25% for 8 patients with adenocarcinoma* *treated with a single dose of 70 mg/m2 of 15 evaluable patients with* *metastatic pulmonary tumor, no patients showed any objective responses. The* *hematologic toxicities were *thrombocytopenia* (less than 5 X* *10(4)/mm3, 41.6%) and *leukocytopenia* (less than 2000/mm3, 28.1%); it* *was observed in 19% of the patients, that *thrombocytopenia* continued* *for more than 6 weeks after stopping therapy. Gastrointestinal symptoms* *such as anorexia (81%), nausea (66%) and vomiting (16%) were severe in* *patients treated with a single dose of 70 mg/m2. Fever in 19%, alopecia in* *13%, phlebitis in 9%, eruption in 6%, stomatitis in 6% and liver* *insufficiency in 13% were also observed.*
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* 12/3,AB/91*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04125220 83255036 PMID: 6820877*
* [Case of malignant melanoma of the external genitalia responding* *satisfactorily to a combination of local injection of OK-432 and* *chemotherapy]*
* Satoh S; Suzuki A; Okamura H; Nishimura T*
* Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jan *1982*, 9* * (1) p140-5, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* A 59-year-old woman with recurrent malignant melanoma of the vulva has* *well responded to a combination of immunotherapy and chemotherapy. As an* *immunotherapy, 10KE OK-432 were injected into the tumor twice a week.* *Chemotherapeutic regimen consisted of intravenous push of 1 mg vincristine* *on day 1,100 mg dacarbazine from day 1 through 5 and 50 mg nitrosourea* *(ACNU) on day 5. This treatment was repeated with 4 week intervals. Before* *treatment, the patient had a 3 X 3 X 5 cm subcutaneous mass on the left* *vaginal wall near the introitus. Fifty percent objective reduction of the* *tumor was achieved 6 weeks after commencement of intralegional* *immunotherapy and chemotherapy, and the tumor almost disappeared 8 months* *later. At this time, the treatment was changed to a supportive* *immunotherapy with intramuscular injection of 1KE OK-432 twice a week. But* *the tumor began to enlarge 2 months later and the patient is now being* *treated with the same combination therapy. Major side effects were febrile* *episodes on the day of intratumor injection of OK-432 and nausea, vomiting* *during the interval of chemotherapy. Anemia was the main hematologic side* *effect, but *leukocytopenia* and *thrombocytopenia* were not* *severe. The combination of intratumor injection of OK-432 and chemotherapy* *seems to be effective for the treatment of malignant melanoma.* **
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* 12/3,AB/92*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04125215 83255031 PMID: 6820875*
* [MQF-OK therapy in advanced terminal stomach cancer--with special* *reference to a comparison with MFC therapy]*
* Sakata Y; Yoshida Y; Komatsu Y; Sugawara K; Nishimura S; Kikuchi K* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) Jan *1982*, 9* * (1) p109-15, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Sakata, et al. has already reported that the combination therapy of* *mitomycin-C, carboquone, 5-fluorouracil and OK-432 (MQF-OK therapy) which* *had established from animal experiments, was exceedingly effective for* *inoperable human gastric cancer. In this paper, the effectiveness of MQF-OK* *therapy for inoperable gastric cancer was compared with that of MFC* *therapy. To perform this controlled study, a "large area" co-operative* *study group of cancer chemotherapy, composed of 14 institutions in Aomori* *and a part of Akita prefectures, was organized. From April 1977 to April*

*1980, patients were registered and 61 cases were evaluable; 31 out of 61* *were treated with MQF-OK therapy (MQF-OK group) and the others with MFC* *group. The background of the cases, such as sex, age etc, was not different* *significantly between two groups statistically. According to the response* *criteria of Japan Society for Cancer Therapy, 18 cases out of 31 cases of* *MQF-OK group and 9 of 30 cases of MFC group showed "improvement." According* *to Karnofsky's criteria 17 cases of MQF-OK group and 8 of MFC group showed* *effectiveness more than I-A, respectively. There was a statistical* *significance between the two groups (P less than 0.001). By Kaplan-Meier's* *method, the MQF-OK group survived longer than the MFC group (P = 0.05). The* *complications, such as *leukocytopenia*, *thrombocytopenia* or* *gastrointestinal complaints, were more frequently found in MQF-OK-432 group* *than in MFC group (P less than 0.05). But these complications decreased or* *resolved spontaneously 1 to 4 weeks after the administration of MQF-OK* *therapy. On these results, MQF-OK therapy was considered excellent method* *for treatment of inoperable gastric cancer and will be furthermore* *attempted against other cancers.*
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* 12/3,AB/93*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04125159 83254975 PMID: 6575725*
* [Clinical effects of human lymphoblastoid interferon in patients with* *hematologic neoplasms]*
* Oda Y; Irie S; Inagaki M; Fukumoto M; Ueda I; Ohmoto E; Fujimoto S; Endo* *Y; Watanabe S; Lai M; Takahashi I; Kimura I; Ishii H; Sezaki T* * Gan to kagaku ryoho. Cancer & chemotherapy (JAPAN) May *1983*, 10* * (5) p1313-9, ISSN 0385-0684 Journal Code: 7810034* * Document type: Journal Article ; English Abstract*
* Languages: JAPANESE*
* Main Citation Owner: NLM*
* Record type: Completed*
* Sixteen patients with hematologic neoplasms were treated with Human* *Lymphoblastoid Interferon (HL-BI) derived from Namalwa cell line. They were* *6 multiple myeloma, 8 acute leukemia and 2 malignant lymphoma patients. All* *patients were previously treated with anticancer agents except one case* *with multiple myeloma. HLBI, 3.0 X 10(6) IU/day, was daily administered by* *intramuscular injection at least for 4 weeks. Three of 6 multiple myeloma* *responded to HLBI with a decrease of more than 25% in serum myeloma protein* *level. A case with pleural effusion due to massive infiltration of myeloma* *cells treated with intrathoratic administration of HLBI, in whom complete* *disappearance of pleural effusion was recognized. On the other hand, no* *patients with acute leukemia and malignant lymphoma responded except one* *case with acute lymphocytic leukemia, in which bone marrow lymphoblasts* *decreased transiently. Fever episodes, 13 of 16 cases, were more frequently* *seen but were manageable. Transient *leukocytopenia* and* **thrombocytopenia* were also observed in 4 and 7 of 8 cases,* *respectively. No anaphylactoid reaction was seen. Thus, HLBI was expected* *useful in the clinical management of multiple myeloma.* **
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* 12/3,AB/94*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*04122634 83252407 PMID: 6307001*
* Combination chemotherapy for small cell carcinoma of the lung: evaluation* *of four-drug combination of cyclophosphamide, vincristine, methotrexate,* *and procarbazine.*
* Ohnoshi T; Hiraki S; Nakata Y; Machida K; Fujii M; Nakata Y; Murakami N;* *Miyake K; Harada J; Ozawa S; Seto T; Tamura T; Kimura I* * Acta medica Okayama (JAPAN) Apr *1983*, 37 (2) p147-53, ISSN* *0386-300X Journal Code: 0417611*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Forty-one patients with small cell carcinoma of the lung were treated* *with a four-drug combination of cyclophosphamide, vincristine,* *methotrexate, and procarbazine. The response rate was 68% (28 responded* *among 41 patients), with 10 complete responses (24%) and 18 partial* *responses (44%). The median survival time from the initiation of* *chemotherapy was 11 months for patients with limited disease and 8 months* *for those with extensive disease. Patients who achieved complete response* *survived significantly longer than those who did not; the median survival* *time for complete responders was 14.5 months, compared to 8.5 months for* *partial responders and 6 months for non-responders. Myelosuppressive* *toxicity remained within acceptable limits, with 5% incidence of* **leukocytopenia* (less than 1,000/microliter) and 7% incidence of* **thrombocytopenia* (less than 50,000/microliter) following the first* *course of the regimen.*
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* 12/3,AB/95*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*03499355 81191132 PMID: 7228457*
* Increased danger of bone marrow damage in simultaneous* *azathioprine-allopurinol therapy.*

* Zazgornik J; Kopsa H; Schmidt P; Pils P; Kuschan K; Deutsch E* * International journal of clinical pharmacology, therapy, and toxicology (* *GERMANY, WEST) Mar *1981*, 19 (3) p96-7, ISSN 0174-4879* *Journal Code: 8003415*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* Two renal transplant recipients with reversible bone marrow damage in the* *course of a simultaneous azathioprine-allopurinol therapy are discussed.* *Anemia, *leukocytopenia* and *thrombocytopenia* were found in both* *patients. Discontinuation of the azathioprine-allopurinol treatment was* *followed by increase of hematocrit, hemoglobin, erythrocytes, white blood* *cells and platelets. Interaction of azathioprine and allopurinol seems to* *be responsible for bone marrow damage in these patients. It can be* *concluded that the dose of azathioprine should be reduced when allopurinol* *is given concomitantly.*
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* 12/3,AB/96*
*DIALOG(R)File 155:MEDLINE(R)*
*(c) format only 2003 The Dialog Corp. All rts. reserv.* **
*02781987 78211759 PMID: 667366*
* Oxymetholone treatment in myelofibrosis.*
* Hast R; Engstedt L; Jameson S; Killander A; Lundh B; Reizenstein P;* *Skarberg K O; Uden A M; Wadman B*
* Blut (GERMANY, WEST) Jul 14 *1978*, 37 (1) p19-26, ISSN* *0006-5242 Journal Code: 0173401*
* Document type: Journal Article*
* Languages: ENGLISH*
* Main Citation Owner: NLM*
* Record type: Completed*
* In order to study the effect of oxymetholone therapy in advanced* *myelofibrosis, 11 patients (4 females, 7 males) were given, 3--5 mg per kg* *body weight, long-term oxymetholone treatment in a prospective multicenter* *study. Five cases had previously had a diagnosis of polycythemia vera. All* *patients had anemia initially, 4 *leukocytopenia* and 10* **thrombocytopenia* in addition. Hepato-splenomegaly was present in all* *cases but in varying degree. Five patients required regular blood* *transfusions before treatment. In 9 of the 15 courses given, there was* *normalization of the peripheral blood or substantial improvement (better* *than 3 g hemoglobin/dl or 50 X 10(9) platelets/1) after androgens.* *Significant effects were noted both on hemoglobin values and platelet* *counts. The need for blood transfusions ceased completely in all 5 cases.* *When oxymetholone treatment was reduced or interrupted 4 patients relapsed;* *2 of them responded to a renewed course. The red cell counts returned to* *previous polycythemic values in one patient and another died from acute* *leukemia. The results of this study suggest that androgens might be of* *value in advanced cases of myelofibrosis with transfusion-requiring anemia* *or severe *thrombocytopenia*.*
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* 12/3,AB/97*
*DIALOG(R)File 155:MEDLINE(R)*
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*02175355 76129488 PMID: 1215885*
* [Familial Wilson's disease: copper induced hemolysis, hypersplenism and* *hyperpigmentation as the main symptoms]*
* Familiarer Morbus Wilson: kupferinduzierte Hamolyse, Hyperspleniesyndrom* *und Hyperpigmentation als Leitsymptome*
* Steiner P; Frey P; Lupi G A; Kistler H J*
* Schweizerische medizinische Wochenschrift (SWITZERLAND) Jul 5* **1975*, 105 (27) p872-9, ISSN 0036-7672 Journal Code: 0404401* * Document type: Journal Article ; English Abstract*
* Languages: GERMAN*
* Main Citation Owner: NLM*
* Record type: Completed*
* Wilson's disease was diagnosed in a 16-year-old adolescent who presented* *with signs of hypersplenism due to cirrhosis, with marked hyperpigmentation* *of both lower legs and neurological disturbances. In view of progressive* **thrombocytopenia* and *leukocytopenia*, splenectomy was performed* *during therapy with penicillamine later in the course, and the result was* *good. The patient's 12-year-old sister was found to have a hepatic form of* *Wilson's disease with typical biochemical findings. During the initial* *hospitalization a severe, spontaneous copper-induced hemolysis was noted.* *Another sister probably has a presymptomatic form of the disease. The* *parents are healthy but heterozygote carriers with regard to biochemical* *findings. The importance is stressed of hypersplenism, hyperpigmentation of* *the legs and especially of acute hemolysis in infancy as pointers in the* *diagnosis of Wilson's disease. Further diagnostic and therapeutic aspects* *are discussed.*
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* 12/3,AB/98*
*DIALOG(R)File 155:MEDLINE(R)*
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*02082387 76033687 PMID: 1166294*
* [Drug allergy damage to the blood ]*
* Medikamentos-allergische Schaden des Blutes*
* Muller U*
* Schweizerische medizinische Wochenschrift (SWITZERLAND) Aug 23* **1975*, 105 (34)